ABSTRACTS OF WORLD MEDICINE

VOL. 27 NO. 2 FEBRUARY, 1960

Pathology

243. **Measurement of Free Acid in Gastric Juice by Means of Indicator Paper**

I. I. SIPPY and E. J. FITZSIMONS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1157–1158, July 4, 1959. 5 refs.

In this paper from the Northwestern University Medical School and Wesley Memorial Hospital, Chicago, the authors report an investigation of the usefulness of a single indicator paper having a broad colour scale between *p*H 1 and *p*H 6 for estimating the amount of free hydrochloric acid in gastric juice. For purposes of comparison the amount of free acid in several samples of gastric juice was determined by standard methods. There was a good correlation between the degrees of free acid and *p*H measured by titration and the *p*H measured with the single indicator paper.

H. Lehmann

EXPERIMENTAL PATHOLOGY

244. **The Effect of Fever on Temperature Regulation in Men**

R. K. MACPHERSON. *Clinical Science* [*Clin. Sci.*] **18**, 281–287, May [received Sept.], 1959. 3 figs., 4 refs.

A subject who was engaged in a series of experiments in which he was exposed to varying levels of heat stress in a climatic chamber, suffered from a respiratory tract infection accompanied by fever but continued to participate in the experiments. It was observed that during the course of his illness his rectal and mean skin temperatures during the experiments accurately reproduced the expected patterns but at a new higher level determined by the height of his fever. His sweat loss was unaffected. It was concluded that at moderate levels of fever body temperature-regulation is unimpaired.—[Author's summary.]

245. **The Composition of Cigarette Smoke: Studies on Stubs and Tips**

A. J. LINDSEY. *British Journal of Cancer* [*Brit. J. Cancer*] **13**, 195–199, June [received Sept.], 1959. 1 fig., 9 refs.

Studies have been made of the total amounts of condensible smoke produced at various stages in the smoking of cigarettes and it has been demonstrated that the stubs retain large quantities of such condensible matter. The amounts are in harmony with the idea of a succession of distillation processes during the smoking sequence.

The smoke from cigarettes smoked to long and short stubs was analysed for polycyclic aromatic hydrocarbons and it was shown that from the same number of cigarettes four times as much 3:4-benzpyrene was found in the smoke when short stubs were left as when long ones were discarded. This is in harmony with statistical studies of lung cancer mortality and stub length in smoking populations. Smoking to a short stub has less effect on the amounts of other hydrocarbons. Tips were also studied and it was shown that they retain far less polycyclic aromatic hydrocarbons than stubs of similar length.—[Author's summary.]

246. **Experimental Pulmonary *Pneumocystis carinii* Infection in Rabbits**

W. H. SHELDON. *Journal of Experimental Medicine* [*J. exp. Med.*] **110**, 147–160, July, 1959. 10 figs., 20 refs.

Interstitial plasma-cell pneumonia due to *Pneumocystis carinii* is well known in Europe, but only recently have reports of cases begun to appear in the North American literature. In this paper from Emory University School of Medicine, Atlanta, the author, who has previously described 4 cases of a subclinical form of the infection discovered post mortem (*A.M.A. J. Dis. Child.*, 1959, **97**, 287; *Abstr. Wld Med.*, 1959, **26**, 195), now describes an attempt to reproduce the disease in rabbits.

The 54 animals used were divided into four major groups. (1) After treatment with cortisone and antibiotics (penicillin and streptomycin) 20 rabbits were inoculated intranasally with a suspension prepared from frozen lung tissue obtained either from a typical human case of the disease or from a rabbit previously inoculated with human material; (2) 12 rabbits similarly treated with cortisone and antibiotics were inoculated with saline or boiled normal human lung; (3) 9 animals treated with antibiotics only, without cortisone, were inoculated with the infected lung suspension; and (4) 13 remained untreated and uninoculated and served as controls. [There is a discrepancy in the protocols relating to 3 animals in the last group.] Individual members of large litters were distributed equally among the different groups.

The degree of infection in the 6 animals which died and also in the remainder (which were killed at varying times up to 33 days from the start of the experiment) was assessed in terms of the number of cysts of *Pneumocystis* in lung smears and the extent of the histological changes in the lungs. The latter, even in animals showing the most severe infection, consisted in interstitial pneumoni-

tis only, there being neither generalized intra-alveolar honeycomb exudate nor interstitial plasma-cell infiltration such as has been frequently described in the typical lesions of *Pneumocystis* pneumonia in infants. The most marked lesions were found in Groups 1 and 2 and were of about the same severity in both these groups. Animals in Group 3 showed less marked changes, while the control group was least affected of all, though even in this group organisms were seen in smears from 11 animals and minimal pneumonitic lesions in 7. The author concludes that latent *Pneumocystis* infection was widespread in his rabbits, and that transmission of the disease could not therefore be established. He considers that suppression of resistance in the hosts by cortisone permitted the activation of latent infection, but not to the degree seen in the typical condition in infants. *E. G. Hall*

247. **Observations on the Intrapulmonary Accumulation of Acid Mucopolysaccharides.** (Наблюдения по поводу внутрилегочных накоплений кислых мукополисахаридов)
N. G. Lupu, K. Velikan, and D. Velikan. *Архив Патологии* [*Arh. Patol.*] **21**, 51–59, No. 6, 1959. 8 figs., 6 refs.

In the course of histological studies of pulmonary fibrosis carried out at the Therapeutic Institute, Bucharest, the presence in a proportion of macrophages of metachromatic substances was noted, as well as the presence of similarly staining aggregates in the connective tissue of the lungs.

In the present study, which was undertaken in order to throw further light on this finding, pulmonary fibrosis was induced in 400 guinea-pigs by means of pure silicon dioxide, tobacco smoke, exogenous histamine, and electrically induced endogenous histamine. Under the influence of these substances a marked increase was observed in the number of macrophages containing metachromatic material (on staining with toluidine blue or periodic-acid–Schiff); this material later also appeared as a rim around these cells. Histochemically, the metachromatic substance was proved to be an acid mucopolysaccharide. It was observed that "pre-collagen" fibres later developed in this pericellular metachromatic substance in pulmonary connective tissue. Finally it was demonstrated that formation of the substance can be inhibited and prevented by the administration of synthetic antihistaminics before exposure to the noxious agent. *A. Swan*

248. **The Histopathology of Experimental Infections by Intestinal Neurotropic Viruses.** (Гистопатология экспериментальных инфекций, вызванных заражением кишечными невротропными вирусами)
I. A. Robinzon, M. P. Frolova, A. P. Savinov, and M. A. Šeftel. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **59**, 769–776, No. 7, 1959. 4 figs., 11 refs.

In these experimental studies 19 monkeys were infected with poliomyelitis virus Type AB isolated from the faeces of patients suffering from the disease in Karaganda, while 5 more monkeys were infected with Coxsackie virus Type A7. In addition, over 100 rodents (chiefly cotton rats and white mice) were infected with these same viral strains. The AB strain of poliovirus as well as 2 other strains (MK and G3) isolated in the same epidemic differ in their immunological reactions from the classic Types 1, 2, and 3 and have been grouped together as Type 4; these strains, with the Coxsackie virus A7, have peculiarities common to viruses of the Coxsackie group as a whole in addition to those they share with the poliomyelitis group (Types 1, 2, and 3). Thus they are pathogenic to suckling white mice and rats as well as to monkeys and they are myotropic as well as neurotropic. The lesions they cause in the central nervous system, however, are more diffuse and are associated with a greater mesenchymal reaction than are the commoner polioviruses. This neurotropism is most evident in suckling cotton rats and less marked in suckling white mice. In monkeys and rodents alike the lesions are not confined to the cells of the anterior horn, for the pontine nuclei and the motor, frontal, post-central, islet, and temporal cortex are often attacked.

It is suggested therefore that these strains should be regarded as a group on its own, distinct from the main group of Coxsackie viruses on the one hand and from the three common types of poliomyelitis virus on the other. It appears from the work of Dalldorf that this applies also to the Coxsackie virus A14.

L. Firman-Edwards

HAEMATOLOGY

249. **On the Problem of Naturally Occurring Leukocyte Agglutinins.** [In English]
S.-Å. Killmann. *Acta medica Scandinavica* [*Acta med. scand.*] **163**, 445–448, 1959. 12 refs.

At Rigshospitalet, Copenhagen, sera from 50 persons without a history of blood transfusion and free from diseases associated with the presence of leucocyte antibodies were examined for such antibodies by a modification of Dausset's technique against a panel of seven different leucocytes. None were detected.

The relevant literature is reviewed and it is concluded that the bulk of the evidence is against the existence of naturally occurring antibodies to leucocytes.

I. Dunsford

250. **On the Occurrence of Leukocyte Agglutinins. A Comparative Study of 374 Patients.** [In English]
S.-Å. Killmann. *Acta medica Scandinavica* [*Acta med. scand.*] **163**, 449–465, 1959. 1 fig., 26 refs.

Sera from 374 patients suffering from haematological or collagen diseases were examined at Rigshopitalet, Copenhagen, by a modification of Dausset's technique for the presence of leucocyte antibodies, which were found in 71 cases. Differences were found between the leucocyte agglutinins present in the collagen diseases and those present in other diseases. The antibodies in cases of the former group are considered to be of a special type, apparently occurring without antigenic stimulus and not being significantly associated with leucopenia or neutropenia. In cases of the latter group

on the other hand a history of transfusion is a major characteristic, and the leucopenia and neutropenia found in some of the author's cases and in those reported by others suggest that some of the antibodies may be auto-antibodies directed against the patient's own leucocytes. No conclusive evidence was obtained to suggest that leucocyte antibodies can be formed as a result of pregnancy.

[This is an extensive paper and worthy of study by those interested in this particular field.] *I. Dunsford*

251. **Relationship of Blood Protein Composition to Intravascular Erythrocyte Aggregation (Sludged Blood).** [Monograph, in English]
J. DITZEL. *Acta medica Scandinavica* [*Acta med. scand.*] 164, Suppl. 343, 1–63, 1959. 17 figs., bibliography.

252. **The Macrocytosis of Hepatic Disease. I. Thin Macrocytosis**
J. BINGHAM. *Blood* [*Blood*] **14**, 694–707, June, 1959. 4 figs., 13 refs.

Disease of the liver is often associated with macrocytosis. In the course of this study, which was undertaken at the University of Toronto in order to re-examine the problem by studying a large group of patients suffering from various types of hepatic and biliary diseases, it became apparent that there was not one type of macrocyte but three, and that each type could occur alone or in combination with one or both of the others in various proportions. The three types were termed "thin", "thick", and "target" macrocytes respectively; in the present paper the author discusses the thin macrocytes in detail.

Of 222 patients with hepatic disease of various kinds, the erythrocytes were of normal size in 55, in 30 they were of normal mean cell diameter (M.C.D.) but there was increased anisocytosis, indicating that both macrocytes and microcytes were present, while in 137 cases (62%) the erythrocytes had a M.C.D. of 7·6 μ or more. These last were the patients considered to have a macrocytic blood picture (macrocytosis); 81 of them (59%) showed thin macrocytes, 39 (29%) target macrocytes, and 17 (12%) thick macrocytes. A thin macrocyte is defined as one having an increased M.C.D. (7·6 μ or more), a decrease in thickness, and a normal volume; thus compared with the normal erythrocyte it is a "flattened" cell. As the flattening becomes greater, so the diameter of the cell increases. Patients with this type of macrocytosis were not suffering from severe anaemia. Examination of the bone marrow in 27 cases revealed the presence of macronormoblasts in 26 and megaloblasts in one. Blood transfusion studies were carried out on 4 patients and on 4 control subjects; when normal-sized erythrocytes were transfused into patients with thin macrocytosis the donor cells did not become macrocytic. Hence it is concluded that there was no factor in the peripheral cell circulation of the patients with macrocytosis responsible for altering the shape of the erythrocytes. Thin macrocytosis was found in the blood of patients with all types of hepatic disease, except in those with fatty infiltration of the liver or obstructive jaundice of short duration. It is suggested that the important aetiological factor is damage to the hepatic parenchymal cells, from any cause. *H. Lehmann*

MORBID ANATOMY AND CYTOLOGY

253. **Simple Cerebral Scars: Intrinsic Cortical Circulation and Its Relation to Focal Vascular Lesions**
C. B. COURVILLE. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] 67, 660–669, June, 1959. 6 figs., 9 refs.

The author reports from the Cajal Laboratory of Neuropathology, Los Angeles County Hospital, a study of the structure and mechanism of formation of cerebral cortical scars, which are generally assumed to be a residual effect of vascular disease causing obstruction. For this purpose he used his own modification of the Laidlaw silver technique for the demonstration of reticulin. By this method the clearing of sections 250 μ in thickness makes it possible to demonstrate the finer cortical vasculature in 3 dimensions. After a lengthy discussion of the normal vascular supply of the cortex the author points out that cortical scars of vascular origin are due either to arterial obstruction or to venous thrombosis; only those due to the former cause are considered in this paper—which is based on a study of only 12 cases and is therefore described as "introductory".

Nevertheless, a classification is put forward and the vascular components of the lesion described. They are usually "deficit scars", causing distortion only of the immediate cortex involved. If the vessel is small and no great amount of nervous tissue is lost they form a local capillary complex. If, however, a larger artery is occluded and breakdown of any sizeable mass of cortex occurs a thin glial scar with a reduction in the number of blood vessels results. Such scars may arise for example from occlusion of the penetrating cerebral arteries and assume a vertical orientation, thus resulting in a local vertical scar. A laminar scar extending horizontally for a variable distance in all diameters is usually the result of anoxaemia consequent to a vascular obstruction. Such scars may be extensive and highly vascularized. The changes in the blood vessels responsible for the production of these scars are, however, very variable. There is often proliferation and transformation of the neuroglia and of reticulin.

[This paper does not lend itself to abstracting and should be read in the original.] *R. Wyburn-Mason*

254. **Hypertensive Fibrinoid Arteritis of the Brain and Gross Cerebral Hemorrhage—a Form of "Hyalinosis"**
I. FEIGIN and P. PROSE. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] 1, 98–110, July, 1959. 9 figs., 46 refs.

The authors, writing from New York University–Bellevue Medical Center, New York, describe a type of arteritis of cerebral vessels which they believe to be characteristic of hypertensive disease. Whereas in normotensive brains hyaline change due to collagen replacement is frequently met with, in hypertensive

patients an additional vascular lesion occurs, which they term a fibrinoid type of hyaline, in which material with the staining properties of fibrin infiltrates the vessel wall. Inflammatory changes and evidence of old and recent small haemorrhages accompany this change, and it proceeds to collagen replacement. The authors did not find fibrinoid change of this type in organs other than the brain, and they regard it as a pertinent correlation that in hypertension serious haemorrhage occurs only in brain, retina, and nasal mucosa. They consider these lesions to be analogous to the vessel changes in experimental hypertension, and note that the latter may be diminished in intensity by a low-salt diet.

J. B. Cavanagh

255. **Hydranencephaly and Allied Disorders: a Study of Cerebral Defect in Chinese Children**

C. S. Muir. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 231–246, June [received Aug.], 1959. 25 figs., 37 refs.

Hydranencephaly is a condition which was defined by Potter as the complete or almost complete absence of the cerebral hemispheres; the leptomeninges and the dura, however, are completely formed and occupy their normal position in the skull. In this paper from the University of Malaya the author reports the detailed morbid anatomical and histological findings in 6 complete and 5 incomplete examples of this condition, all of which occurred in children of Chinese stock. (Most previously reported cases of this condition have been in infants of Caucasian stock.) In a search of his department's necropsy records for the past 10 years the author found no examples among the numerous Indian, Pakistani, Sikh, and Malayan subjects examined. The literature is reviewed.

In the present cases only very brief clinical records were available; most of the patients died soon after admission from pneumonic infections, and the neurological lesions appeared to be largely unsuspected. In 6 cases the classic picture of complete hydranencephaly was seen, namely, absence of the hemispheres, but with normal, small or enlarged basal ganglia, normal cerebellum, normal dura- and pia-arachnoid, and normal (although small) cerebral blood vessels. There was, however, a variable amount of haemosiderosis both on the surface and deep within the remaining brain substance. In the remaining 5 cases the anomalies were of the same type, though less extensive, consisting in a bizarre malformation and fusion of the frontal lobes in one case, agenesis of one hemisphere in a second case, some degree of porencephaly in 2 cases, and in the 5th case a defect in the temporo-parietal region on one side, with free communication between the lateral ventricle and the surface, and absence of the Sylvian artery.

The aetiology of the condition is discussed in relation to embryological development and in the light of the views of previous authors and the present author's own findings. It is concluded that some unknown noxious factor operating just before the end of the second month of foetal life which interferes with the development of the neural mantle could well produce all the findings observed, with the possible exception of the haemosiderosin pigment. This last feature could best be attributed to cerebral haemorrhage or thrombosis in early foetal life, but the complete absence of vascular lesions at the time of death seems to militate against this theory. In the present stage of knowledge the problem of aetiology cannot yet be resolved.

[The article is profusely illustrated with good photographs of the macroscopic and microscopical findings. It is a pity that the clinical picture cannot be correlated with the excellent detailed description of the pathological findings.] *John Lorber*

256. **Diagnostic Cortical Biopsy: a Histological and Chemical Study**

W. Blackwood and J. N. Cumings. *Lancet* [*Lancet*] **2**, 23–24, July 11, 1959. 5 refs.

The authors report, from the National Hospital, Queen Square, London, the results of 65 diagnostic biopsies of the cerebral hemisphere in various diseases. The biopsies were in each case taken from a presumably diseased cerebral hemisphere, usually from the frontal lobe. Of the 65 specimens, 56 were from children or young adults with increasing mental disability, which was regarded as essential to justify the procedure, and 9 from adults with dementia. The authors state that no patient was worse for the operative procedure. The biopsy was obtained by trephining, a cube of tissue at least 1·5 cm. long and including both grey and white matter being taken. The specimen was divided into two, one part being fixed in formalin and examined histologically by various staining methods, while the other was frozen and examined chemically with Scharlach R, toluidine blue, and periodic-acid–Schiff tests. From 36 specimens a definite diagnosis was made. In some instances the histological and chemical examinations were in agreement, in others only one method was diagnostic; 23 specimens showed no abnormality. In one case conflicting diagnoses were obtained by the two methods. In 3 out of every 4 abnormal biopsies it was possible to make a definite diagnosis by the combined examination.

The authors discuss the features of the biopsy material in 2 difficult cases. They suggest that their procedure is a valuable addition to diagnostic methods in certain cases of dementia. *R. Wyburn-Mason*

257. **The Structure of the Pulmonary Trunk at Different Ages and in Cases of Pulmonary Hypertension and Pulmonary Stenosis**

D. Heath, J. W. DuShane, J. E. Edwards, and E. H. Wood. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **77**, 443–456, 1959. 5 figs., 9 refs.

The authors report from the Mayo Clinic, Rochester, Minnesota, the histological findings in a post-mortem study of the pulmonary trunk in five groups of subjects: (1) normal controls aged 0 to 80 years (including 6 foetuses); (2) 26 cases of congenital and (3) 18 cases of acquired pulmonary hypertension; (4) 12 cases of pulmonary stenosis with intact ventricular septum; and (5) 19 cases of pulmonary stenosis associated with ventricular septal defect (tetrad of Fallot). Pulmonary

hypertension was defined as a pulmonary arterial pressure over 33 mm. Hg.

In the normal foetus the mediae of the pulmonary trunk and of the aorta are of the same thickness and the configuration of elastic tissue in them is similar, the fibres being long, uniform, and arranged tangentially. The foetal pulmonary trunk may be said to have an "aortic configuration". About 6 months after birth the relative thickness of the media of the pulmonary artery decreases and the elastica becomes fragmented and less compact, the fibrils remaining parallel and of uniform width; this configuration of elastica is designated "transitional". By the end of the second year of life the "adult pulmonary" type of elastic configuration is established, the fibres now being short and irregular in shape and distribution. In all 18 cases of acquired pulmonary hypertension the media of the pulmonary trunk showed "adult pulmonary" configuration. All except one of the 26 cases of congenital pulmonary hypertension showed "aortic configuration". Of the 12 cases of pulmonary stenosis without ventricular septal defect the configuration was of a "chronic hypotensive" type, that is, displaying either very thin and sparse elastic fibres or irregular isolated masses of elastic tissue. Of those in Group 5, 9 had transitional configuration and in 10 it was of the adult type; some of these patients in whom the pulmonary stenosis was associated with ventricular septal defect, although aged 8 years, still showed the "aortic configuration", suggesting that in these cases transition to the adult type of configuration is delayed.

The authors conclude (1) that the form and arrangement of elastic tissue of an artery are closely related to intravascular pressure; and (2) that there is no fixed association between pulmonary stenosis of unspecified degree and any particular configuration of elastic tissue in the pulmonary trunk, which is determined "rather by the levels of blood pressure and flow in the pulmonary circulation and is related to the thickness of the vessel". They consider that the classic term "tetralogy of Fallot" has "no specific functional connotation", and suggest that the descriptions "large ventricular septal defect with severe pulmonary stenosis" and "large ventricular septal defect with slight pulmonary stenosis" would provide a clearer conception of the physiological conditions actually present and of their clinical significance.

H. Caplan

258. **Asian Influenzal Pneumonitis: a Structural and Virologic Analysis**

P. J. SOTO, G. O. BROUN, and J. P. WYATT. *American Journal of Medicine* [*Amer. J. Med.*] **27**, 18–25, July, 1959. 8 figs., 9 refs.

Virological, bacteriological, and detailed pathological studies were carried out on 9 patients dying from fulminant Asian influenzal pneumonia in the St. Louis University group of hospitals. The Asian influenza virus was isolated from lung tissue in 6 instances, and the diagnosis was established in the remaining 3 cases from the characteristic post-mortem lung changes. There was a haemorrhagic bronchopneumonia with alveolar oedema and a well developed eosinophilic, band-like, hyaline membrane, in sharp contrast to the congested septal walls. Within the membrane sudanophilic vacuoles with an associated foreign-body reaction led to its fragmentation and disruption. The authors consider that this lipid material is derived from serum escaping through injured capillaries and that the basic constituent of the hyaline membrane comes from serum globulin. This membrane was sufficient to cause a mechanical alveolo-capillary block resulting in death from anoxaemia. Contributory factors were bacterial infection and pre-existing disease, the latter including myocardial ischaemia, mitral stenosis, and hepatic cirrhosis; in addition 4 of the patients were pregnant. Derangement of the cardio-pulmonary circulation by any of these conditions could only be adversely affected still further by fulminant viral and bacterial infection, particularly since the infection was asphyxial in type.

D. Geraint James

259. **Cardiovascular Factors in Development of Pulmonary Hyaline Membrane**

D. R. SHANKLIN. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **68**, 49–57, July, 1959. 1 fig., 18 refs.

This communication from Duke University Medical Center, Durham, N. Carolina, is mainly devoted to a discussion of the possible influence of circulatory factors in the production of hyaline membrane in the lungs of premature newborn infants, the author basing his arguments on a study of the records of 335 premature infants born between 1930 and 1955 whose birth weights varied between 500 and 2,500 g. and who all lived at least one hour, but less than 120 hours (5 days), after birth. Excluding 11 infants delivered by caesarean section—among whom the incidence of hyaline membrane was 72% (8 cases)—the remaining 324 cases were divided into three groups: (1) 34 infants showing cardiac malformations; (2) 34 with a heart weight greater than 1·5 times the normal for their birth weight; and (3) the residual group of 256 infants, who were regarded as controls.

The incidence of hyaline membrane in the whole series was 39·4%, and in the three groups 79·5, 65·0, and 29·3% respectively. In an analysis made within the groups according to birth weight the most significant finding was in the control group, in which there was an appreciably lower incidence of hyaline membrane in those infants with birth weights between 500 and 1,000 g. than in the rest. The development of the author's thesis is based on a further consideration of Groups 1 and 3. Histological studies of lung sections from cases of hyaline membrane in Group 3 (controls) showed a high incidence of pulmonary vascular congestion and atelectasis, but in no instance was hyaline membrane present in the absence of oedema, an observation which the author considers highly significant and from which he concludes that the membrane develops by condensation of, and precipitation from, oedema fluid.

To explain the greater frequency of hyaline membrane in premature than in full-term normal infants the author brings forward evidence which he interprets as indicating that there is a greater difference in strength between the right and left ventricles in the premature infant than in

the full-term infant, the consequent relative inadequacy of the left ventricle in the former resulting in flooding of the pulmonary vascular bed, with the development of oedema and subsequently hyaline membrane. The argument is supported by an analysis of the 34 cases in which cardiac malformations were present. Hyaline membrane occurred in almost every case in which such abnormality would be likely to lead to overloading of the pulmonary circulation, but did not appear when the abnormality would cause diminished pulmonary blood flow. The author considers other factors influencing the dynamics of the pulmonary circulation; he finally concludes that atelectasis is the primary lesion in initiating a train of events which leads through cardiac failure to pulmonary oedema, and that hyaline membrane is significant only as the end-product of precipitation of oedema fluid.

[This interesting paper does not lend itself to abstracting and should be read in full by those interested in the subject.] *E. G. Hall*

260. **Exfoliative Cytology in Metastatic Cancer of the Lung**

B. F. Rosenberg, H. J. Spjut, and M. M. Gedney. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 226–231, July 30, 1959. 5 figs., 6 refs.

Cytological examination of the sputum or bronchial washings was carried out in 50 cases of suspected metastatic carcinoma of the lung admitted to Barnes Hospital, St. Louis, Missouri, between 1948 and 1958. Malignant cells were found in the sputum in 8 cases, in bronchial washings in 7 cases, and in both sputum and bronchial washings in 4. In 8 of these 19 cases the findings on bronchoscopy were normal. The authors briefly describe 4 cases in which metastatic carcinoma of the lung was diagnosed only from the cytological findings. The primary sources were carcinoma of the cervix uteri, breast, gastro-intestinal tract, and skin, and sarcoma.

The authors consider that there is a definite place for the cytological examination of sputum or bronchial washings in all patients with cancer who have pulmonary symptoms or an asymptomatic lesion in the chest on x-ray examination. *H. Caplan*

261. **Cholangiolocellular Carcinoma of the Liver**

P. E. Steiner and J. Higginson. *Cancer* [*Cancer (Philad.)*] **12**, 753–759, July–Aug., 1959. 6 figs., 17 refs.

The authors put forward the view that there are rare types of liver carcinoma histologically resembling the cholangioles—that is, the structures connecting the bile canaliculi with the interlobar bile ducts—and propose for these the term " cholangiolocellular " carcinoma of the liver. Amongst over 1,000 American and African cases of cancer of the liver they encountered this type of neoplasm 11 times, corresponding to a frequency of about 1%. The sex ratio was 4 in women to 7 in men, thus resembling that of cholangiocellular carcinoma; and the average age was 50 years, with a range from 22 to 64 years.

In most of the cases the liver was enlarged, the average weight being 3,000 g., and cirrhosis was usually absent. Macroscopically, the growth presented as numerous small yellowish nodules in part of or throughout the entire organ, showing some tendency towards confluence. Metastases were present in 7 of the 10 cases that came to necropsy, involving mainly the portal lymph nodes and lungs and less frequently other organs. Histologically, the neoplasm presented as thin solid cords, occasionally displaying miniature lumina, made up of flat or cuboidal anaplastic epithelial cells embedded in abundant oedematous stroma. Reticulum fibres were demonstrable surrounding the tumour cells. In some cases continuity between tumour cells and atrophic hepatic cells or bile ducts was observed, and this was interpreted as supporting the authors' view that the growths probably arose from the terminal bile ductules. *R. Salm*

262. **Inclusion-bearing Cells in the Urine in Certain Viral Infections**

R. P. Bolande. *Pediatrics* [*Pediatrics*] **24**, 7–12, July, 1959. 3 figs., 11 refs.

The finding of large cells containing cytoplasmic inclusions resembling viral inclusion bodies in the urine of an apparently well child who later developed measles led the author, at Western Reserve University, Cleveland, Ohio, to study the urine of patients with common viral infections to determine the occurrence and significance of such cells. The infections included measles, German measles, chicken-pox, mumps, herpangina, and aseptic meningitis. In nearly all cases inclusion-bearing cells were present in the urine. The inclusion-bearing cell is described as a round cell, 15 to 40 μ in diameter, with one to three pyknotic eccentric nuclei. The cytoplasmic inclusion is round or oval, 5 to 10 μ in diameter, hyalo-refractile, and sharply demarcated from the surrounding cytoplasm. It is not refractile in polarized light. It stains brightly eosinophilic, though the degree of eosinophilia may vary and at times shifts to a basophilic greenish hue. Inclusion-bearing cells may be detected by low-power scanning.

The inclusion bodies are morphologically similar in all the above-mentioned virus infections, but the number per slide varies considerably, they being most numerous in the prodromal or eruptive stages of measles. Their presence is not pathognomonic of virus infections, for they were occasionally observed in the urine of control patients with meningococcal infections, hyperbilirubinaemia, pyelonephritis, papilloma, and carcinoma of the bladder, and even that of apparently healthy children. However, when found in these control cases the inclusion bodies were small, sparse, and poorly developed. *D. Geraint James*

263. **Diabetic Glomerulosclerosis: Electron and Light Microscopic Studies**

M. G. Farquhar, J. Hopper Jr., and H. D. Moon. *American Journal of Pathology* [*Amer. J. Path.*] **35**, 721–753, July–Aug., 1959. 24 figs., 38 refs.

In a study of diabetic glomerulosclerosis at the University of California School of Medicine, San Francisco, renal biopsy specimens from 7 patients with diabetes mellitus were examined by light and electron microscopy.

There were 6 females and one male aged between 21 and 49 years. Two patients had the classic Kimmelstiel–Wilson syndrome; the remaining 5 had normal renal function and were normotensive.

By light microscopy diabetic glomerulosclerosis was seen to be characterized by gradual obliteration of the glomeruli by deposition of hyaline. The earliest lesions occurred in the primary bifurcations of the afferent arterioles. Hyaline deposition subsequently extended radially to involve all the glomerular loops. Electron microscopy showed that the earliest manifestation of the disorder is a thickening of the basement membrane, and this was demonstrable in glomeruli which had appeared normal by light microscopy. The hyaline deposits were found to be extracellular, lying between adjacent endothelial cells rather than in the intercapillary space as originally proposed by Kimmelstiel and Wilson. Islands of endothelial cells appeared isolated by the expanding masses of hyaline. Finally the capillary lumen was obliterated. The hyaline nodular lesion was formed from the diffuse lesion and differed from it only in size and shape. Deposits of fibrinoid which constituted the "exudative lesions" of glomeruli were found in 2 patients with the most advanced glomerular changes. These deposits lay between the basement membrane and the endothelial cell membrane. Comparison showed the fine structural alterations which occurred in the glomeruli in diabetes mellitus to be distinct from those occurring in disseminated lupus erythematosus, nephrosis, amyloidosis, and pre-eclampsia and eclampsia. *A. W. H. Foxell*

264. **Nonatheromatous Peripheral Vascular Disease of the Lower Extremity in Diabetes Mellitus**
S. GOLDENBERG, M. ALEX, R. A. JOSHI, and H. T. BLUMENTHAL. *Diabetes* [*Diabetes*] **8**, 261–273, July–Aug., 1959. 12 figs., 45 refs.

Peripheral vascular disease of the lower limb in diabetes was studied at the Jewish Hospital, St. Louis, Missouri, in 152 amputation specimens (92 from diabetic patients and 60 from patients with various other conditions necessitating amputation).

A lesion of smaller arteries and arterioles is described which appeared to have a causal relationship to diabetes, the digital artery being the largest vessel in which this "diabetic" lesion could be distinguished. The most prominent feature of the lesion was an endothelial proliferation which might almost occlude the lumen. With periodic-acid–Schiff (P.A.S.) stain numerous small fibrillae were seen forming a reticulated pattern, which was colloidal-iron negative, between the endothelial cells. The internal elastic lamina consisted in a single intact wavy membrane, and the media and adventitia remained essentially normal. There was no tendency towards calcification. By contrast, the lesions of arteriosclerosis were characterized by deposition of hyaline material and fraying and reduplication of the internal elastic lamina; the latter also sometimes contained P.A.S.-positive material which was usually colloidal-iron positive.

A study of the clinical findings, where these were available, in all the diabetic and non-diabetic patients with gangrene showed that massive gangrene of the lower limb was more characteristic of the non-diabetic patient with occlusive vascular disease, while a patchy distribution was more characteristically found in the diabetic. On the other hand sharply demarcated gangrene involving all or most of the foot occurred about equally in both groups. In about half of a group of 62 diabetic patients retinopathy and nephropathy could have been associated on clinical grounds with diabetic gangrene. All these complications, it is suggested, may occur in patients considered to have clinically mild, well controlled diabetes. *A. W. H. Foxell*

265. **Lesions of Joints and Tendon Sheaths in Systemic Lupus Erythematosus**
B. CRUIKSHANK. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **18**, 111–119, June [received Sept.], 1959. 14 figs., 28 refs.

The occurrence of joint changes in disseminated lupus erythematosus (D.L.E.) which are clinically and radiologically similar to those found in rheumatoid arthritis has frequently been described. In this paper from Glasgow Royal Infirmary the author details the relevant histological findings in 14 joints taken at necropsy from 10 patients with a histologically confirmed diagnosis of D.L.E. [It is not stated whether L.E. cells were present.] In addition to the joints the palmar flexor tendons were examined in 7 cases. All except one of the 10 patients had had clinical arthritis.

Macroscopically, there was early pannus formation in 2 knees and acute synovitis in another, while the remaining joints showed minimal changes. Histological changes were found in all but one of the joints examined. Fibrin-like material (which the author prefers to call fibrinoid rather than fibrin) was seen on or immediately beneath the synovial surface. In the main the number of synovial cells was reduced, but there were some surfaces with normal or excessive numbers of these cells. Inflammatory cells were inconspicuous. Haematoxylin bodies were found in the synovia of 11 joints. In one patient marked vascular changes were observed; D.L.E. was present together with polyarteritis nodosa in this case, lesions of both conditions being seen in the knee-joint examined. Another patient showed venous thrombosis. In 5 of the 6 finger-joints examined there were cartilage erosion and pannus. These features resembled those of rheumatoid arthritis, but were apparently less severe. Six cases of tendon-sheath involvement were seen. Changes were like those found in the synovial membranes, but with a more pronounced inflammatory element. The author claims that, when viewed collectively, these histological changes can serve to differentiate the arthritis of D.L.E. from other forms of arthritis.

[Some of the illustrations, especially of the finger-joints, show appearances which are very difficult to differentiate from those of rheumatoid arthritis. Clinical details of these cases would have been helpful. The finding of tenosynovitis and the high incidence of synovial haematoxylin bodies are of considerable interest.] *G. Loewi*

Microbiology and Parasitology

266. **The Systematic Histological Examination of the Central Nervous System of Biting Animals.** (A propos des examens histologiques systématiques des névraxes d'animaux mordeurs)
R. BÉQUIGNON, G. SERGENT, and C. VIALAT. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **96**, 702–711, June, 1959. 18 figs., 19 refs.

The systematic histological examination of the central nervous system of animals—principally dogs—which have bitten human beings and are suspected of rabies is an essential preliminary to the institution of serum therapy or anti-rabies vaccination. The risk involved in such treatment, though small, is none the less real, and it should not be undertaken unless the diagnosis in the animal has been adequately confirmed. The authors, writing from the Pasteur Institute, Paris, draw attention to the fact that toxoplasmosis may cause an encephalitis in domestic animals which, in certain cases, is indistinguishable clinically from rabies. They point out that the Negri bodies characteristic of rabies were in the past regarded as protozoal by many authorities—including Negri himself—owing to their histological appearance and to their resemblance to various other inclusion bodies, of undoubted protozoal origin, which have been found in cells of the central nervous system of animals. In the authors' opinion many of these inclusion bodies, described under various names, actually represent different stages in the life-cycle of *Toxoplasma gondii*. The hypothetical protozoal origin of rabies has finally been disproved by electron microscopy of the Negri bodies. But despite their similar appearance the distinction between Negri bodies and protozoal bodies can be made by optical microscopy.

The authors' experience shows that at the present time *T. gondii* is a particularly frequent cause of acute encephalitis in cats and dogs in France, the organisms being readily found in the brain cells, though inflammatory lesions are always limited in extent and there is no perivasculitis. During the three years 1956–8 the brains of 342 dogs and 98 cats suspected of rabies were examined at the Pasteur Institute. The findings were normal in 16 dogs and 8 cats and rabies was diagnosed in 31 dogs and 2 cats, but in no fewer than 295 dogs and 88 cats evidence of toxoplasmosis was found. This was confirmed by intraperitoneal inoculation into mice, in which naturally acquired toxoplasmosis is rare in laboratory-bred strains. [Some very interesting photomicrographs are reproduced.]

[From this paper, coming from a source which must surely be as authoritative as any in the world, it is evident that toxoplasmosis must always be included in the differential diagnosis of rabies in animals and that the histological examination of the brain for Negri bodies, with all its implications for those at risk, is a matter requiring continuous practice. The figures reported must inevitably have general repercussions on statistics of the results of anti-rabies treatment. The paper should be read in full by all responsible for, or interested in, the diagnosis of rabies.] *W. K. Dunscombe*

267. **Microbial Sensitivity Test in Management of Urinary Tract Infections**
K. A. MIAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 934–938, June 20, 1959. 2 figs., 10 refs.

The author, reporting from the St. Joseph Mercy Hospital, Ann Arbor, Michigan, describes a new method for determining the antibiotic sensitivity of bacteria causing urinary-tract infections. In a Petri dish is placed a "base layer" of melted medium (beef-heart–calf-brain–potato infusion, proteose peptone, sodium chloride, disodium phosphate, dextrose, agar) in which is incorporated 15% whole citrated human blood. After solidification a "seed layer" consisting of melted medium plus sediment from the centrifuged sample of urine is poured over the base layer. Antibiotic disks are placed on the seed layer and the dish is incubated at 37° C. The oxyhaemoglobin of the blood is reduced by the seed layer containing the inoculum of micro-organisms and the colour of the blood changes from bright red to purple. Interpretation of the results depends on the presence or absence of distinct bright-red zones of inhibition round the disks. Results of 70% of tests could be read in 2 to 4 hours, of 92% within 6 hours, and only 2·8% required overnight incubation. Methods are described in detail. Patients with urinary-tract infections refractory to prolonged empirical therapy responded quickly to treatment based on this method of testing the antibiotic sensitivity of the causal organisms.

The incidence of the more frequent urinary-tract pathogens found during 1953–8 in 6,870 cultures was as follows: *Escherichia* 38·5%, *Pseudomonas* 6·6%, *Aerobacter* 5·1%, *Proteus* 18·5%, *Streptococcus* (*Enterococcus*) 18·2%, *Staphylococcus pyogenes* (*albus* and *aureus*) 6·8%. *Joyce Wright*

268. **Intracellular Survival of Staphylococci**
F. A. KAPRAL and M. G. SHAYEGANI. *Journal of Experimental Medicine* [*J. exp. Med.*] **110**, 123–138, July, 1959. 10 figs., 9 refs.

The authors describe a tissue-culture procedure developed at the School of Medicine, University of Pennsylvania, Philadelphia, to follow quantitatively the intracellular survival of staphylococci within leucocytes. The technique is as follows. Staphylococci are added to suspensions of rabbit or rat mononuclear cells in Hanks's medium containing 20% homologous serum and enough streptomycin to inhibit extracellular growth of the organisms. The suspensions are incubated in "perspex" cells with coverslips, to which the mononuclears adhere. At intervals the coverslips are removed and ground up with glass beads in the presence of saponin.

The number of surviving staphylococci in the monocytes is enumerated by explantation on to agar. By this method it was possible to show that virulent *Staphylococcus aureus* is taken up by rabbit monocytes but survives without multiplication, whereas *Staph. albus* is killed. Rat monocytes, on the other hand, killed both species of staphylococci. *R. Hare*

269. **The Kinetic Seroneutralization Reaction with Poliomyelitis Virus.** (La réaction cinétique de séroneutralisation des virus poliomyélitiques)
P. LÉPINE, F. ROGER, and A. ROGER. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **20**, 563–578, 1959. 14 refs.

The authors, writing from the Institut Pasteur, Paris, describe in full practical detail an *in-vitro* neutralization test for poliomyelitis antibodies in human serum. Various dilutions of virus suspension are incubated with the test serum for 3 hours at 37° C. and a suspension of human buccal epithelioma cells (Type KB) grown in an enriched casein hydrolysate is then added. The tubes are examined for lysis of the cells after 48 and 72 hours. The test is simpler than the customary one using monkey kidney and allows many more sera to be examined in a short time. *M. Lubran*

270. **Q Fever Studies. XX. Comparison of Four Serologic Techniques for the Detection and Measurement of Antibody to *Coxiella burnetti* in Naturally Exposed Sheep**
E. H. WELSH, F. W. JENSEN, and E. H. LENNETTE. *American Journal of Hygiene* [*Amer. J. Hyg.*] **70**, 1–13, July, 1959. 13 refs.

This paper from the Viral and Rickettsial Disease Laboratory, Berkeley, California, is based on a 3-year study of the natural spread of Q fever through a flock of sheep numbering 840. Although 284 (87%) of the 328 animals on which information was most complete were known to have excreted *Rickettsia burneti* at one or more of three parturitions, only 163 (50%) had demonstrable complement-fixing antibodies in the serum at some time during the observation period. Because of this disparity other methods of testing for antibodies were used to provide a comparison with the complement-fixation test (C.F.T.). These were: (1) the standard rickettsial agglutination test (S.R.A.T.), (2) the capillary agglutination test (C.A.T.), and (3) the microscopic slide agglutination test (M.S.A.T.). Details of these tests and of the C.F.T. previously used are given. The comparative study was carried out on 1,017 sera collected by serial bleedings from 113 sheep. Preliminary tests showed that heat inactivation of sera or the addition of 1:10,000 thiomersal had no effect on the results obtained by any of the methods used for comparison, so that the initial treatment of specimens was simplified.

Although 97 (86%) of the 113 animals were known to have excreted *R. burneti*, only 60 (53%) had detectable antibodies as shown by the C.F.T. The results obtained with the S.R.A.T. (68 positive, or 60%) and the C.A.T. (65 positive, or 58%) were not greatly different if a titre of 1:8 is accepted as significant. The M.S.A.T., however, gave a much higher rate of positive results (111, or 98%). The authors consider this to be due to its greater specificity rather than to an increase in non-specific positive results, basing their opinion on their knowledge of the rickettsial excretion pattern in the flock combined with the opportunities for multiple exposure to infection. *A. E. Wright*

271. **Studies on the Antibody Response in Splenectomized Persons**
S. SASLAW, B. A. BOURONCLE, R. L. WALL, and C. A. DOAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 120–125, July 16, 1959. 2 figs., 19 refs.

This paper from Ohio State University College of Medicine, Columbus, describes a study of the antibody response to subcutaneously administered tularaemia vaccine in 105 subjects who had undergone splenectomy (selected at random) and 47 healthy control subjects. These 152 subjects were divided into two groups: Group 1, consisting of 48 splenectomized patients and 15 controls, received only one injection of 0·5 ml. of the vaccine, while Group 2, containing 57 and 32 subjects respectively, were given three injections each of 0·5 ml. on successive days. Blood for serological and electrophoretic studies was taken before immunization and at weekly intervals for 5 weeks subsequently.

In Group 1, 8 of the 48 patients (7 out of 31 females and one out of 17 males) did not produce a specific antibody response to the vaccine, whereas all 15 controls did so. In Group 2, 52 of the 57 patients produced antibodies, only 5 (4 out of 39 females and one out of 19 males) failing to do so; all the controls again showed an antibody response. Thus 13 out of 105 splenectomized persons failed to develop specific antibodies after immunization. These included 2 out of 37 with idiopathic thrombocytopenic purpura, 5 out of 23 with congenital haemolytic anaemia, one out of 13 with acquired haemolytic anaemia, both of 2 patients with anaemia secondary to chronic lymphatic leukaemia, one out of 8 with splenic neutropenia, one out of 5 with splenic panhaematopenia, and one patient with aplastic anaemia. It is noteworthy that all 6 patients with traumatic rupture of the spleen showed an antibody response, since these were the only patients who could be truly compared with healthy controls. As the authors remark, ideally the controls should have intact spleens but be suffering from the same underlying diseases as those for which the patients underwent splenectomy. A small pilot study of 10 such subjects showed that only 6 of the 10 produced an antibody response, those failing to do so being 2 patients with chronic lymphatic leukaemia, one out of 3 with primary splenic neutropenia, and a patient with acute monoblastic leukaemia. These results suggest that failure to produce antibodies is related to the underlying disease rather than to the absence of the spleen. The sex of the patient may also possibly influence the antibody response, since 13 out of 73 females compared with only 4 out of 42 males showed no antibody response.

Filter-paper strip electrophoresis failed to reveal any correlation between the serum electrophoretic pattern and the antibody response in either the splenectomized patients or the normal control subjects. *I. Berkinshaw-Smith*

Pharmacology and Therapeutics

272. **A New Nonamphetamine Anorectic Agent**
S. C. Freed and E. E. Hays. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **238**, 55–59, July, 1959. 1 fig., 6 refs.

A new long-acting anorectic drug, 2-phenyl-*tert.*-butylamine resinate (" ionamin "), which is considered to have advantages over the amphetamine compounds in the management of obesity by suppressing appetite, was given to a series of 178 patients, the multiple-dose technique being used. The dosage ranged from 15 to 60 mg. daily according to the sensitivity of the patient, and the effect lasted for 8 to 9 hours. There was an average weight loss of 0·25 lb. (113 g.) per patient per day. Toxic symptoms, which were mild, included insomnia without tension, nausea, and dry mouth. Nervousness and agitation occurred in only 3 of the patients. The authors conclude that ionamin effectively suppresses appetite with a significantly lower incidence of side-effects than amphetamine in equivalent dosage. *R. Schneider*

273. **Peritoneal Dialysis. I. Technique and Applications**
M. H. Maxwell, R. E. Rockney, C. R. Kleeman, and M. R. Twiss. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 917–924, June 20, 1959. 3 figs.

At the University of California Medical Center, Los Angeles, peritoneal dialysis was successfully carried out on 76 occasions on patients suffering from acute renal failure, barbiturate poisoning, intractable oedema, hepatic coma, hypercalcaemia, and chronic uraemia. The solution was prepared commercially and had the following composition in mEq. per litre: sodium 140, chloride 101, calcium 4, magnesium 1·5, and lactate 45, with dextrose 15 g. per litre. Where required 4 mEq. of potassium chloride per litre was added. This solution was allowed to run into the abdominal cavity under gravity through a nylon catheter (0·136 inch (3·45 mm.) external diameter) with a solid rounded tip, the last 3 inches (7·6 cm.) of which were perforated with 80 smooth holes 0·02 inch (0·5 mm.) in diameter. The catheter was introduced through a metal trocar. The fluid was allowed to remain in the peritoneum for one hour and then siphoned off by placing the delivery bottles on the floor. Fresh bottles and tubes were then connected and the process repeated up to a recommended maximum of 36 hours. In some instances there was abdominal pain, especially towards the end of the outflow period, but this could be relieved by instillation through the catheter of 5 ml. of a 2% procaine solution. Abdominal distension and ileus were not prominent. The only contraindications were peritoneal infection and recent or extensive surgery.

The method, although not so efficient as the artificial kidney, is simple and can be used without specialized knowledge of fluid and electrolyte metabolism and without intricate laboratory facilities. *Norval Taylor*

274. **" Kendozid " in the Treatment of Heart Failure.**
(Лечение больных с недостаточностью кровообращения кендозидом)
D. Ja. Bezman. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **37**, 127–130, July, 1959.

The author describes a new Soviet preparation, " kendozid ", which is obtained from the root of *Apocynum cannabinum* and which increases the force of contraction of the myocardial muscle, slows cardiac rhythm, and prolongs diastole. Its effect is not cumulative and like strophanthin it acts rapidly; unlike strophanthin, however, it stimulates the respiratory centre. In a trial on 49 patients (33 men and 16 women) of various ages, including 22 with mitral disease, 5 with aortic and mitral lesions, 14 with atherosclerotic heart disease, and 8 with cor pulmonale, this preparation was given in a course of 10 to 15 slow intravenous infusions of 0·5 ml. on the first day and 1 ml. on subsequent days in 20 ml. of a 20% solution of glucose. The following data were then recorded: the degree of subjective improvement, degree and intensity of dyspnoea and orthopnoea, changes affecting appetite, sleep, mood, pulse rate, diuresis, pulse pressure, exudates, oedema, and pulse deficit, amount of pulmonary and hepatic congestion, and the electrocardiographic and radiological findings.

Considerable and persistent improvement was observed in 7 patients with 2nd-degree heart failure, none of these requiring readmission to hospital during the 2 years following the treatment. Of a further 31 patients with 2nd-degree failure, 27 showed rapid and satisfactory improvement. Of 11 patients with 3rd-degree failure, 9 responded slowly and incompletely, but showed some degree of improvement lasting 1 to 3 months. Lastly, of 4 patients with recurrent endocarditis and rheumatic attacks and 2nd-degree failure, one who had atherosclerotic heart disease and another with cor pulmonale failed to respond to this or any of the older cardiotonic drugs. Kendozid was also of benefit in heart failure with associated coronary insufficiency since it does not cause constriction of the coronary vessels. No complications of the treatment were observed. In cases of very severe heart failure the course of kendozid infusions was followed or augmented by digitalis therapy. The results of such combined therapy were better than those obtained with either drug alone. *S. W. Waydenfeld*

275. **Effects of a New " Coronary Vasodilator " on the General and Coronary Hemodynamics and Myocardial Metabolism of Man**
E. Traks, D. B. Hackel, and S. M. Sancetta. *Annals of Internal Medicine* [*Ann. intern. Med.*] **51**, 31–38, July, 1959. 13 refs.

The effect of " basoflex " (N-cinnamylmethylamino-2-phenylpropane hydrochloride), a synthetic substance chemically related to the catechol amines, on the heart

rate, blood pressure, cardiac output, and coronary blood flow was studied in patients at the Cleveland Metropolitan General Hospital, Ohio. The drug was given intravenously in a dose of 0·5 mg. per kg. body weight over a period of 3 minutes, and samples of blood from the brachial artery and coronary sinus were analysed for oxygen, glucose, lactate, and pyruvate concentrations. The mean values for the heart rate and blood pressure, determined in 14 patients in a recumbent position, were not affected by the drug during 45 minutes following administration. In 6 patients the mean cardiac output (determined by the Fick principle with oxygen) and the left ventricular work were increased 8 minutes after vasoflex was given. The coronary blood flow and the left ventricular oxygen consumption were significantly increased by the drug. There were no significant changes in the arterial levels or percentage extractions of glucose, lactate, and pyruvate, but the left ventricular utilization of these substances increased. It was confirmed in 4 anaesthetized dogs that vasoflex did not alter the oxygen tension in the tissue of the myocardium.

It was concluded that the increased coronary blood flow produced by vasoflex balanced rather than exceeded an increased myocardial oxygen demand.

P. A. Nasmyth

276. **A New, Potent Antihypertensive Drug: Preliminary Study of [2-(Octahydro-1-azocinyl)-ethyl]-guanidine Sulfate (Guanethidine)**
J. H. Page and H. P. Dustan. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1265–1271, July 11, 1959. 5 figs., 7 refs.

Two new antihypertensive drugs—[2-(octahydro-1-azocinyl)-ethyl]-guanidine sulphate (SU 5864; guanethidine) and hexahydro-1-azepinepropionamidoxime dihydrochloride (SU 4029)—were studied both clinically and experimentally at the Cleveland Clinic Foundation and Frank E. Bunts Educational Institute, Cleveland, Ohio. Guanethidine was given for periods of 2 to 12 weeks to 18 patients with hypertension, therapy with either reserpine or chlorothiazide, or both, being continued at the same time in 7 cases. Of the 18 patients, 16 had a decrease in both standing and supine blood pressure; in the other 2 cases only the standing blood pressure was reduced. Orthostatic hypotension was severe in some cases, but it tended to become less troublesome and in only 2 cases was reduction in dosage necessary. In no case did tolerance to the antihypertensive effect of the drug develop. Decreases in blood pressure were noted within 4 hours of the initial dose, although in some cases the effects were delayed for a week or more. The initial daily dose was between 25 and 100 mg., and the dosage required to maintain satisfactory blood-pressure reduction ranged from 25 mg. on alternate days to 150 mg. 3 times daily. Side-effects included diarrhoea and bradycardia, which occurred in 8 and 9 cases respectively.

SU 4029 was given to 8 hypertensive patients. In only 2 of these was there a significant fall in supine blood pressure, and in both cases fever developed. Six of the 8 patients had postural hypotension and one developed diffuse myalgia.

In the experimental part of the investigation intravenous administration of guanethidine caused a fall in blood pressure in healthy dogs under pentobarbitone anaesthesia, but not in unanaesthetized healthy dogs. The cardiac output (as judged by the aortic flow measured by an electromagnetic flowmeter) markedly increased when the drug was given intravenously to unanaesthetized dogs. A sustained rise in blood pressure occurred within the vessels of the perfused, denervated hind legs of dogs when guanethidine was injected. The drug also suppressed the carotid occlusion reflex in anaesthetized dogs after vagal section. Injection of guanethidine modified the response of both anaesthetized and unanaesthetized dogs to pressor or depressor drugs, the effect of vasopressin and similar drugs being augmented, whereas that of amphetamine, ephedrine, and similar drugs was usually depressed. In dogs with experimentally produced renal hypertension the hypotensive effect of intravenously administered guanethidine was short and followed by a prolonged pressor effect. In dogs with experimentally produced neurogenic hypertension given the drug by mouth the depressor effect was marked and prolonged.

P. T. Main

277. **Darenthin: Hypotensive Agent of New Type**
A. L. A. Boura, A. F. Green, A. McCoubrey, D. R. Laurence, R. Moulton, and M. L. Rosenheim. *Lancet* [*Lancet*] **2**, 17–21, July 11, 1959. 6 figs., 4 refs.

From University College Hospital Medical School, London, the authors describe the pharmacology of "darenthin" (bretylium tosilate), a benzyl quarternary ammonium compound. This new agent is capable of blocking the peripheral sympathetic (adrenergic) nervous system without antagonizing the effects of released or injected adrenaline or noradrenaline. In experimental studies it was shown that darenthin causes postural hypotension in anaesthetized cats, this being preceded, if the intravenous dose is a large one, by hypertension; it inhibits cardiac acceleration when the inferior cardiac branch of the sympathetic system is stimulated, and contraction of the nictitating membrane when the cervical sympathetic is stimulated, and it increases the pressor response and that of the nictitating membrane to adrenaline and noradrenaline. It has no action on the parasympathetic nervous system and does not block the pressor effect caused by activating the adrenal medulla by splanchnic nerve stimulation. Unlike reserpine it does not, when administered daily, deplete the catechol amine content of the adrenal medulla or sympathetic ganglia. A study of the distribution of darenthin labelled with radioactive carbon showed that the drug was concentrated in the sympathetic ganglia, post-ganglionic sympathetic fibres, and organs with a rich adrenergic innervation. It was only partly absorbed from the intestine and was excreted in the urine fairly rapidly, 10 to 30% being recovered. Tolerance to large daily doses was soon acquired, the reactions to the drug becoming progressively less, possibly in a manner resembling the diminishing effects of sympathectomy. Acute toxicity occurred at 30 times the sympatholytic dose, probably as a result of neuromuscular block. No chronic toxic effects were observed after administration

for 4 to 6 weeks to rats, cats, and monkeys. Since noradrenaline, and to a lesser extent adrenaline, showed a greater pressor effect when given after darenthin, and since, unlike the ganglion-blocking agents, darenthin does not block the mechanism of release of these catechol amines from the adrenal medulla, the activity of the adrenal medulla may be expected to influence blood pressure and various sympathetic functions to a relatively greater extent after administration of the compound.

In normal human volunteer subjects there was some variation in the dose required to cause postural hypotension; a dose of 53 mg. given intravenously was effective in one subject, but not in another. Very severe hypertension developed in a patient with phaeochromocytoma after the cautious intravenous administration of 53 mg. Orally, 131 mg. was effective in one normal subject, but 328 mg. had no effect in another; the onset of hypotension occurred 1½ to 3 hours after administration and lasted for 8 hours. Partial or complete nasal obstruction occurred in a majority of tests. Of 3 hypertensive patients, a dose of 37 mg. intravenously caused postural hypotension in 2 which was maximal in 1 to 2 hours and lasted up to 8 hours; in the third patient 94 mg. produced no effect. When given orally in doses of 197 to 328 mg. the drug reduced the blood pressure in 3 out of 4 hypertensive patients in 1½ to 3 hours, the effect lasting up to 9 hours. There was much individual variation in susceptibility as between patients, and in some several episodes of severe postural hypotension occurred, probably owing to irregularities of absorption.

A further trial was carried out on 36 hypertensive patients, of whom 10 had not previously undergone hypotensive therapy, 20 had received ganglion-blocking agents, and 5 reserpine. The effective dose varied from 130 to 840 mg. 8-hourly; the latter dose, which was never exceeded, failed in one subject. One patient with malignant hypertension showed considerable benefit generally, with improvement in the optic fundal appearances. Side-effects were trivial, consisting mainly in mild transitory nasal stuffiness. No discomfort was experienced by two patients with angina, but another patient showed dropped heart beats. The virtual absence of troublesome side-effects represents a considerable advantage over the ganglion-blocking drugs. It seems likely that tolerance to the drug may develop, though it was no problem in the cases studied so far. The authors conclude that darenthin deserves a more extensive trial in the treatment of hypertension. *Bernard J. Freedman*

278. **New Anticoagulant for Oral Use—3-(1′-Phenylpropyl)-4-hydroxycoumarin (Liquamar): Its Evaluation for Short-term Therapy**
H. Gold and G. W. Lilley. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1303–1306, July 11, 1959. 13 refs.

Results of short-term oral anticoagulant therapy of acute vascular disorders with the coumarin derivative 3-(1′-phenylpropyl)-4-hydroxycoumarin (" liquamar "; " marcoumar ") are reported from Chester Hospital, Chester, Pennsylvania. It is pointed out that although this drug has been under investigation for some years in Europe, only a few studies have been reported in the U.S.A. Of the 111 patients now treated, 80 had acute myocardial infarction, 9 coronary insufficiency, 12 acute phlebitis, 5 acute pulmonary infarction, 3 atrial fibrillation with cerebral embolism, 1 atrial fibrillation with iliac arterial embolism, and 1 acute retinal-vein thrombosis. There were 71 males and 40 females aged between 34 and 84 years. The prothrombin time was determined by the Quick one-stage method before treatment was started and again thereafter daily, the dose of the drug being adjusted to keep the prothrombin time within the range 25 to 35 seconds.

With a 30-mg. loading dose of liquamar 77·3% of the patients showed a prophylactic response (prothrombin time 20 to 25 seconds) or therapeutic response (prothrombin time 25 to 35 seconds) within an average of 42 hours. After this period an additional average maintenance dose of 6·4 mg. [presumably daily] led to protective prolongation of prothrombin time in 88% of the patients within 66 hours of administration of the loading dose. The maintenance dose varied from 1·5 mg. to 12 mg. depending on the daily prothrombin-time readings. When the pre-treatment prothrombin time was prolonged above normal a smaller loading dose of 21 mg. was given. If immediate anticoagulant effect was required heparin was also administered. Prolongation of the prothrombin time beyond 40 seconds at some time during treatment was noted in 26·6% of patients, and in 15·2% it occurred within 5 days of the 30-mg. loading dose being given. Vitamin K_1 by mouth in doses of 2·5 to 10 mg. was used to control prolongation of prothrombin time. The vitamin was also given both intravenously and by mouth in a dosage varying between 5 mg. and 50 mg. to counteract episodes of frank bleeding, which occurred in 4 cases (3·6%). Complete recovery from this complication ensued in all 4 cases. *P. T. Main*

279. **The Effects of Bronchodilators on Pulmonary Ventilation and Diffusion in Asthma and Emphysema**
G. Lorriman. *Thorax* [*Thorax*] **14**, 146–152, June, 1959. 3 figs., 35 refs.

The effect of bronchodilators on pulmonary ventilation and diffusion in asthma and emphysema was studied in patients at the Brompton Hospital, London. Most of the asthmatics suffered from intermittent wheezing and dyspnoea; the emphysematous patients were persistently breathless on exertion and had a long history of productive chronic bronchitis. Ventilation was assessed by measuring the forced expiratory volume at one second, and the diffusing capacity for carbon monoxide was estimated by the steady-state technique (Bates *et al.*, *J. Physiol.* (*Lond.*), 1955, **129**, 237).

Inhalations of approximately 0·75 ml. of a 1% aerosol of isoprenaline were given over a period of 1½ minutes to 47 patients. Ventilation and diffusion were estimated before and 8 minutes after treatment. There was an increase in ventilation ranging from 8% to 45%, the increase being much higher in asthmatics than in patients with bronchitis and emphysema and higher in young patients than in patients in the older age groups. There was no significant increase in diffusing capacity.

Prednisolone was given by mouth to 13 patients and corticotrophin gel to one, all of whom were unresponsive to antispasmodics. The dosage of prednisolone and times of testing varied from patient to patient. Clinical improvement was observed in 6 asthmatics, but one asthmatic and 7 patients with bronchitis did not benefit. In those who improved there was a marked increase in both ventilation and diffusion.

The author discusses possible reasons for the increase in ventilation but not of diffusion as a result of inhalation of isoprenaline. He states that prednisolone appears to act by relieving obstruction. Increased diffusion capacity is significant only if minute volume is constant.

D. Goldman

280. **Clinical and Experimental Studies of Hydrochlorothiazide (" Esidrex "), a New Sulphonamide with Diuretic Action.** (Experimentell-klinische Untersuchungen über Hydrochlorothiazid (Esidrex), ein neues diuretisch wirksames Sulfonamid)

E. RICHTERICH. *Klinische Wochenschrift* [*Klin. Wschr.*] 37, 355–365, April 1, 1959. 8 figs., bibliography.

The author reports from the University Medical Clinic, Basle, a trial of the diuretic hydrochlorothiazide in the treatment of 11 patients with oedema due to a mild degree of right ventricular failure who received a sodium-poor diet with the addition of 6 g. of sodium chloride. Dose–response curves were constructed by plotting dose against level of urinary sodium excretion. These curves showed the usual " S " shape, which became a straight line when plotted on a logarithmic scale. The maximally effective dose of hydrochlorothiazide was only 100 mg. compared with 2 g. of chlorothiazide.

Estimations of urinary electrolyte levels in 5 of the patients showed that sodium, chloride, and potassium excretion were all increased. In contrast with the effect of chlorothiazide, however, the rise in potassium excretion was not statistically significant and there was no evidence of a rise in bicarbonate excretion. After administration of chlorothiazide there is a rapid rise in sodium excretion, reaching a maximum at 5 hours and lasting for 9 hours. With hydrochlorothiazide sodium excretion curves show a double peak, first at 4 hours and again at 10 hours, and the effect lasts for 16 hours. In 6 patients without cardiac or renal disease hydrochlorothiazide led to a considerable loss of weight after 2 days' medication, which, however, returned to the original value 3 days after the drug had been stopped. Clearance experiments suggested that hydrochlorothiazide acts mainly by depressing the tubular reabsorption of either sodium or chloride ions.

R. Schneider

281. **Hydrochlorothiazide, a New Oral Diuretic**

M. M. PLATTS. *British Medical Journal* [*Brit. med. J.*] 1, 1565–1568, June 20, 1959. 5 figs., 14 refs.

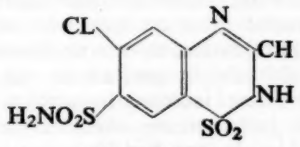
In this paper from the Royal Hospital, Sheffield, a comparative study is reported of the effect of hydrochlorothiazide and of chlorothiazide on urinary water and electrolyte excretion in 3 healthy subjects and 21 patients with congestive heart failure. The patients with heart failure were allowed one litre of fluid and 0·5 g. or 3 g. of sodium chloride a day. The dosage of chlorothiazide was 1 g. a day and that of hydrochlorothiazide 0·1 to 0·4 g. daily. It was found that 0·1 g. of hydrochlorothiazide produced the same diuretic effect as 1 g. of chlorothiazide in patients with congestive heart failure. Excretion of bicarbonate was less with hydrochlorothiazide than with chlorothiazide. The results suggest that hydrochlorothiazide will produce potassium depletion as readily as chlorothiazide.

G. S. Crockett

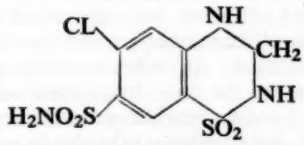
282. **Clinical Evaluation of Hydrochlorothiazide**

C. W. H. HAVARD and J. C. B. FENTON. *British Medical Journal* [*Brit. med. J.*] 1, 1560–1565, June 20, 1959. 3 figs., 15 refs.

At St. Bartholomew's Hospital, London, the effect of hydrochlorothiazide on the urinary excretion of water and electrolytes was studied in 12 patients with oedema of recent onset and 9 with chronic oedema, the results being then compared with those achieved with chlorothiazide. The structural formulae of the two drugs is shown below:



Chlorothiazide



Hydrochlorothiazide

The dosage of chlorothiazide was 0·5 g. twice daily and that of hydrochlorothiazide was 50 mg. twice daily. An interval of 2 to 4 days elapsed between the 4-day course of either drug. Each patient was allowed 1,500 ml. of water and 25 mEq. of sodium a day. The diuretic response to 100 mg. of hydrochlorothiazide was equal to that to 1 g. of chlorothiazide similarly administered and the pattern of electrolyte excretion was the same. Nevertheless, the potassium loss was greater in patients with chronic oedema than in those with oedema of recent origin. The authors suggest that mercurial diuretics may be equally potent in their effect on potassium excretion, but their greater toxicity " prevents their daily administration so that the cumulative effect of a constant potassium diuresis less often progresses to a fall in the serum [potassium] level ".

G. S. Crockett

283. **The Effect of Chlorothiazide on Renal Excretion of Electrolytes and Free Water**

H. O. HEINEMANN, F. E. DEMARTINI, and J. H. LARAGH. *American Journal of Medicine* [*Amer. J. Med.*] **26**, 853–861, June, 1959. 5 figs., 19 refs.

In a comparative study of the diuretic actions of chlorothiazide and the mercurial diuretic meralluride here reported from the Presbyterian Hospital (Columbia

University), New York, the effect of these drugs on the excretion of water and electrolytes was measured in 14 patients with no cardiac or renal disease during a water diuresis induced by the oral administration of 1 litre of water and maintained by intravenous infusion of glucose solution, and also in one patient with diabetes insipidus.

Absorption of electrolytes in the proximal renal tubules is isosmotic. In the distal tubules on the other hand selective absorption of electrolytes occurs in the absence of antidiuretic hormone during water diuresis, allowing free water excretion. In this study it was shown that chlorothiazide produced an increased flow of urine and excretion of solutes, but the free water excretion was unchanged or diminished. Meralluride produced a similar rise in urinary flow and a lesser rise in solute output, but an increased free water excretion. The action of meralluride can thus be explained only by assuming that it causes depression of proximal tubular activity, leaving selective electrolyte reabsorption in the distal tubule unaffected. Chlorothiazide on the other hand impairs both proximal and distal tubular function and so the free water clearance is decreased or unchanged.

The glomerular filtration rate was moderately decreased by chlorothiazide, but was unaffected by meralluride. Chlorothiazide, in contrast to meralluride, produced a significant increase in uric acid clearance. Chlorothiazide had a greater effect on the excretion of sodium and chloride than had the mercurial, and in all patients promoted an increase in potassium excretion; this potassium diuresis was prevented by previous administration of meralluride, which had little effect on potassium excretion. In other respects, however, the diuretic effects of the two drugs were additive. It is suggested that chlorothiazide, with its action on both proximal and distal tubules, should be more effective in sodium-retaining states such as heart failure.

David Phear

284. **Action of Chlorothiazide and "Oradon", Alone and in Combination**

W. J. Poznanski and B. W. Cromie. *British Medical Journal* [*Brit. med. J.*] **1**, 1553–1560, June 20, 1959. 8 figs., 21 refs.

The object of this investigation, which was carried out at the Middlesex Hospital, London, was to determine whether a combination of the mercurial diuretic "oradon" (3-hydroxymercuri-2-methoxyl-1-succinimidopropane theophylline hydrate) and chlorothiazide would produce satisfactory diuresis with a lower incidence of side-effects, particularly of hypokalaemia. A series of 5 patients with persistent oedema, due to congestive cardiac failure in 4 and to the nephrotic syndrome in one, received chlorothiazide in a dosage of 0·5 g. twice daily and oradon in a dosage equivalent to 30 to 60 mg. of mercury daily, about 54% of which was known to be absorbed. Sodium intake was restricted to 25 mEq. daily. The 5 cases are described in detail.

It has already been shown that chlorothiazide produces marked potassium excretion as well as an increase in excretion of salt and water, and that potassium supplements taken at the same time as the chlorothiazide do not necessarily counterbalance the extra loss. In the present study it was found that increased potassium intake was accompanied by a further increase in the excretion rate of the electrolyte if chlorothiazide was also being taken. Thus hypokalaemia can occur although potassium supplements are given. The authors suggest that to counteract the extra potassium loss supplements should be administered on the days when chlorothiazide is not being given. In some cases resistance to chlorothiazide occurred after repeated administration, and raising the dosage did not increase water excretion but did increase potassium excretion. When the two diuretics were given together there was a potentiation effect, but since this applied equally to water and electrolyte excretion no real advantage appears to accrue from combined administration except in cases resistant to the individual drugs.

G. S. Crockett

285. **Amphetamine Sulfate and Athletic Performance: I. Objective Effects**

G. M. Smith and H. K. Beecher. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 542–557, May 30, 1959. 2 refs.

Performances of swimmers, runners, and weight-throwers were compared after they had taken by mouth either 14 mg. of amphetamine per 70 kg. body weight or a placebo 2 to 3 hours before the contests. In further experiments secobarbital (quinalbarbitone) was compared with the placebo in the same way. In all three classes of athletes performance was significantly improved by the amphetamine—3% to 4% in the weight-throwers, 1·5% in the runners, and 0·59% to 1·16% in the swimmers, these improvements being found in about 75% of the subjects. Performance was usually impaired by quinalbarbitone. There are a number of errors both in the tables and in the text of this paper. [For corrections see *J. Amer. med. Ass.*, 1959, **170**, 1432.]

V. J. Woolley

286. **Effect of Amphetamine Sulfate on Athletic Performance**

P. V. Karpovich. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 558–561, May 30, 1959. 3 figs.

Performances were compared in running on a track, on a treadmill, and in swimming before and 30 to 60 minutes after taking 10 or 20 mg. of amphetamine sulphate. Of the 54 students who took part in the tests, only 4 showed any difference in performance as compared with controls given a placebo. Of these, 3 showed an improvement in swimming time and one an impairment in treadmill running. Each of these 4 subjects had received 20 mg. of amphetamine.

V. J. Woolley

287. **An Evaluation of Two New Analgesics (Dextromoramide and Racemoramide) in Healthy Subjects and in Patients with Chronic Pain**

B. Calesnick. *Journal of Chronic Diseases* [*J. chron. Dis.*] **10**, 58–66, July, 1959. 4 figs., 9 refs.

A study of the efficacy of two new analgesics, dextromoramide and racemoramide, which are respectively the dextrorotatory and racemic forms of a substituted

diphenylpropylamine, is reported in this paper from Hahnemann Medical College and St. Joseph's Hospital, Philadelphia.

By determining the pain threshold in 161 healthy young subjects, for which the Wolff–Hardy skin-radiation method was used, the author found that 10 mg. of dextromoramide by mouth was equivalent in analgesic potency to 100 mg. of pethidine or 10 mg. of methadone. Dextromoramide was approximately twice as potent and twice as toxic as racemoramide. In a group of 18 healthy subjects given dextromoramide and racemoramide by mouth there was an increase in the alpha rhythm in the electroencephalogram, indicative of relaxation, and the results of the Rorschach and flashing-light tests indicated greater ease of thought production.

In 18 patients suffering from chronic pain 5 to 10 mg. of dextromoramide or 10 to 20 mg. of racemoramide produced analgesia in about 55 minutes which lasted up to 5 hours with the higher doses. Vertigo, nausea, or drowsiness occurred in 16 patients with these higher doses. Subcutaneous administration of 5 mg. of dextromoramide to 14 patients produced analgesia in 10 to 25 minutes which lasted 2½ to 3½ hours and up to 8 hours in 2 cases. Subcutaneous injection of 10 mg. or 20 mg. caused severe respiratory depression, which was reversed by nalorphine. No instance of primary addiction was observed in a group of 7 patients receiving dextromoramide and racemoramide for several months, but there was evidence of secondary addiction in a morphine–pethidine addict. Side-effects tended to diminish with continued administration.

It is suggested that the drugs may be of value as potent analgesics for oral administration.

[The statistics strongly suggest that the laevorotatory form is quite inactive so far as analgesic potency is concerned.] *T. B. Begg*

288. **The Effects of Meprobamate and Pentobarbitone Sodium on Sleep and Motility during Sleep: a Controlled Trial with Psychiatric Patients**
J. M. Hinton and E. Marley. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **22**, 137–140, May, 1959. 1 fig., 11 refs.

The efficacy of meprobamate as compared with pentobarbitone sodium and a placebo in producing restful sleep was tested in 11 psychiatric patients suffering from hyposomnia at the Maudsley Hospital, London. Of these, 8 were depressive, 2 schizophrenic, and one alcoholic. Each patient was in the trial 18 days. The first 9 days (Series 1) the patient received, for 3 nights each, placebo alternating with 400 mg. and 800 mg. meprobamate. During the second 9 days (Series 2) the effect of 800 mg. meprobamate was compared with that of 200 mg. pentobarbitone sodium. Restlessness was recorded by an electronic device attached to the bed; patients' sleep was also rated by the nurses and by the patients themselves where possible. In Series 1 meprobamate 800 mg. and in Series 2 both meprobamate 800 mg. and pentobarbitone sodium 200 mg. significantly diminished restlessness during sleep. According to the nurses' rating both 400 mg. and 800 mg. meprobamate and 200 mg. pentobarbitone sodium improved sleep. As judged by the patients' own assessments both dosages of meprobamate were effective in Series 1, but only pentobarbitone sodium in Series 2. No good results appeared to follow administration of the placebo.

It is concluded that meprobamate in a dose of 400 mg. is a mild hypnotic and that in a dose of 800 mg. it reduces restlessness, but that in both respects 200 mg. pentobarbitone sodium is more effective. *E. H. Johnson*

289. **The Influence of Drugs on the Psychomotor Aspects of Handwriting.** (Über den Einfluss von Drogen auf die Schreibpsychomotorik)
G. Grünewald. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **198**, 687–704, 1959. 8 figs., 46 refs.

From a study of the effects of drugs on handwriting carried out at the Medical Academy, Düsseldorf, the author suggests that the changes observed can be attributed to a number of basic factors: (1) the motor activation, (2) the degree of relaxation during writing, (3) the inhibition of movement, and (4) the disorganization of movement. It was found that different drugs could produce the same changes in the four factors and their variants, while on the other hand the same drug could produce different changes according to the dosage in which it was given. The changes are considered to be partly due to the primary effects of the drug and partly to the subject's reactions to them, such as counter-regulating mechanisms or compensatory effects. In general the effects can be broadly classified into those which facilitate writing and those which make it more difficult. The former is normally achieved by increased activation or by decrease of inhibition or control of the writing movements, or both may be acting together. Drugs such as methylphenidate hydrochloride (" ritalin "), " peripherin ", and glutamic acid exert a relaxing effect on writing movements if the test subjects are no more than normally tense, but produce an increase in activation in persons who are normally labile, weak, and have irregular handwriting. Disinhibition can also be achieved by spasmolytic drugs. The same effect can be produced by psychogenic alterations in the autonomic nervous system in the direction of restfulness and relaxation. It is therefore always necessary in experiments such as these to take the emotional state, and indeed the total psychological situation, into account. Even changes in the weather can be shown to exert an influence on handwriting and should be allowed for.

The changes which make handwriting more difficult may be due to either inhibition or to disorganization. Drugs producing inhibition include various sedatives, scopolamine, " megaphen ", reserpine, and bromides. Each of these drugs also produces effects peculiar to itself and these are described in detail. Drugs which cause general tiredness in addition to increased inhibition exert a relative disinhibiting and dilatory effect on handwriting which is due to a diminution in controls which in turn leads to disorganization; such an effect is characteristically found in persons under the influence of alcohol. *J. Hoenig*

Chemotherapy

290. **Antibiotics in Fluid Milk. Fourth Nationwide Survey**
W. R. JESTER, W. W. WRIGHT, and H. WELCH. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **9**, 393–397, July, 1959. 5 refs.

Mastitis in cows is usually treated by infusing one or more antibiotic preparations into the udder of the infected animals; residues of these drugs, particularly penicillin, may be secreted with the milk for a time and be ingested by the consumer. In the U.S.A., to determine the incidence of antibiotic residues in milk, market surveys were carried out in 1954, 1955, 1956, and 1959, penicillin being demonstrated in 3·2%, 11·6%, 5·9% and 3·7% of the samples tested in the respective series. A medical advisory panel and other experts met in September, 1956, and agreed that the main public-health problem is the presence of penicillin in milk. Although preparations for the treatment of mastitis may contain other antibiotics, the presence of these in milk does not constitute a public-health problem. Penicillin is a highly active antigenic substance, very small concentrations of which may well cause reactions in hypersensitive consumers, and it is estimated that some 10% of the population may so react. Reactions range from mild, transient rashes to possibly fatal anaphylactic shock, while chronic urticaria and acute dermatitis have been recorded.

If a penicillin-sensitive organism is the cause of the mastitis it is considered that 100,000 units of penicillin will be as effective as larger doses and the drug will disappear more quickly from the milk. In the U.S.A. a warning to the farmer to discard milk for 72 hours after the last treatment must now appear on the label of each immediate container of mastitis preparations.

In the first three surveys referred to above the samples were from milk which had been pooled and processed at the dairies. The 1959 sampling represents a stricter search for penicillin residues in that the milk was taken from tanker lorries leaving the farms or from producers direct.

J. Cauchi

291. **Comparative Study of the Therapeutic Activity of Two New Derivatives of Ethyleneiminobenzoquinone in Certain Malignant Diseases in Man.** (Étude comparée sur des affections tumorales malignes humaines de l'activité thérapeutique de deux nouveaux dérivés de l'éthylène-imine-quinone)
J. BERNARD, G. MATHÉ, and M. WEIL. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **46**, 34–54, Jan.–March [received July], 1959. 16 figs., 8 refs.

Two substituted benzoquinone alkylating agents were selected for trial at the Hôpital Saint-Louis, Paris, because of their good effect in arresting experimental L1210 leukaemia in mice. The first compound, 2:5-methoxyethoxy-3:6-ethyleneimino-1:4-benzoquinine, was given in doses of 10 to 20 mg. daily by mouth to 47 patients with various malignant diseases. Objective improvement occurred in 16 of 20 patients (80%) with Hodgkin's disease and in 9 of 13 patients (69%) with other types of malignant lymphoma such as Brill–Symmers disease. There was also a good response in 7 (87%) of 8 cases of chronic myeloid leukaemia. No effect was noted in 5 patients with various types of carcinoma.

The second substance investigated (in 50 patients) was 2:5-acetamido-3:6-ethyleneimino-1:4-benzoquinone, which was given in the same dose range as the 2:5-methoxyethoxy compound. This substance appeared to be generally less effective in most of the lymphomata and chronic leukaemias, with the possible exception of lymphosarcoma. Of 10 cases of Hodgkin's disease, 6 improved, but to a lesser degree than with the first compound. With neither drug were side-effects significant, although a definite leucopenia developed in about 30% of all cases. It is considered that the 2:5-methoxyethoxy derivative is the more effective, and of particular value in the palliation of Hodgkin's disease.

Kenneth Gurling

292. **Preliminary Results of the Treatment of Certain Malignant Diseases with a Derivative of Ethyleneiminobenzoquinone.** (Résultats préliminaires sur le traitement des affections cancéreuses par une éthylène-iminequinone)
M. BOIRON, J. FAUVET, and C. PAOLETTI. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **46**, 55–74, Jan.–March [received July], 1959. 16 figs.

The therapeutic effect of the alkylating agent 2:5-acetamido-3:6-ethyleneimino-1:4-benzoquinone has been studied in 65 patients with malignant diseases at the Institut G.-Roussy, Villejuif, Seine. The dosage ranged between 10 and 20 mg. daily by mouth for some 3 to 6 weeks, the average total amounts given being between 300 and 600 mg.; the duration of treatment was prolonged to over 10 weeks in a few cases. The drug was well tolerated, but inevitably caused a moderate leucopenia in about one-third of the patients and a slighter degree of thrombocytopenia. Patients with a variety of types of carcinoma showed little response, only 2 out of 38 (5%) improving objectively. Those with sarcoma of bone and soft tissues, other than reticulo-endothelial tissue, also failed to improve. On the other hand objective improvement resulted in 6 out of 12 patients with malignant lymphoma; in these the lymph nodes, liver, and spleen decreased in size, fever diminished, and the patients' general condition improved. This drug is considered to be of value in the treatment of Hodgkin's disease and other diseases of this type.

Kenneth Gurling

Infectious Diseases

293. **Assessment of Respiratory Failure in Poliomyelitis**
R. V. WALLEY. *British Medical Journal* [*Brit. med. J.*] 2, 82–85, July 25, 1959. 1 fig., 20 refs.

This paper describes the author's experience at Ham Green Hospital, Bristol, in treating respiratory failure in 62 cases of poliomyelitis, and reinforces the well-known criteria for assessment. The counting test was found to be a useful guide; in this test the patient is asked to take a deep breath and then to count at the rate of 2 digits a second until forced to take another breath. If he can only count up to 20 his vital capacity has fallen to 2,000 ml.; if he can only reach 15 it is about 1,500 ml., and so on. The dangers of underventilation are stressed; the appearance of cyanosis and the clinical signs of hypercapnia indicate gross hypoventilation. Spirometry, arterial blood gas analysis, end-tidal air CO_2 content, chest radiography, and measurement of positive pressure in the respirator were also employed. The author considers that when the vital capacity falls to a quarter of the predicted normal, assisted respiration is required. This is easier to assess when there is no bulbar involvement. If any weakness in swallowing becomes apparent in addition to respiratory weakness, tracheotomy should be performed. Radiography must then be used to assist clinical assessment to detect lung collapse; a marked difference between end-tidal air CO_2 and arterial CO_2 values is also indicative of collapse.

Residual respiratory paralysis often depends on the state of diaphragmatic function; if this is intact the patient may be little affected, even though the vital capacity is low. If the diaphragm is paralysed exercise tolerance may be poor, although the vital capacity is relatively high. The author confirms the finding of many others that even a mild upper respiratory infection in the recovery period may set the patient back considerably although no signs are heard in the lungs and the radiograph is normal. *D. D. C. Howat*

294. **Herpes Simplex Virus Infection: Dissemination in Association with Malnutrition**
D. MCKENZIE, J. D. L. HANSEN, and W. BECKER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 250–256, June [received Aug.], 1959. 7 figs., 17 refs.

The authors report from the University of Cape Town 8 fatal cases of disseminated herpes simplex infection. This series is unusual inasmuch as it is believed to be the first to be reported from South Africa and also because the patients were aged between 9 and 16 months, and were thus much older than those in previously reported series.

All but one of the children were severely malnourished, while the other main clinical features were severe stomatitis, diarrhoea and vomiting, convulsions, and hepatomegaly. In virus studies performed on various tissues removed at necropsy from 3 of the patients the virus of herpes simplex was isolated from the liver in all 3 cases, from the spleen in 2, and from the lungs in one. (Details of the virological techniques are given.) The most characteristic and, according to the authors, pathognomonic lesions were found in the liver at necropsy in 6 cases. These consisted of pinhead foci of necrosis varying in size from those just visible to the naked eye up to 3 mm. in diameter; they formed a perfect circle, were dead white in colour, and were surrounded by an area of hyperaemia, thus producing a target-like appearance. They were distributed haphazardly throughout the substance of the liver. Similar lesions were found in the tongue and the oesophagus in some of the cases. Microscopically, the lesions were more widely recognizable. Central areas of necrosis were surrounded by dilatation of the sinusoids or by frank haemorrhage, while outside this area inclusion bodies of various ages were found. These are described in great detail.

John Lorber

295. **Disease in Macacus Monkeys Inoculated with ECHO Viruses**
J. H. ARNOLD and J. F. ENDERS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **101**, 513–516, July [received Sept.], 1959. 1 fig., 11 refs.

The experiments described in this paper from the Research Division of Infectious Diseases, Children's Medical Center, Boston, were designed to determine whether 2 types of E.C.H.O. virus—Type 6 Strain SHO and Type 16 Strain HAR—would produce disease in the central nervous system of monkeys, 7 rhesus and 3 cynomolgus monkeys being used. From each animal 1 to 2 ml. of cerebrospinal fluid (C.S.F.) was first withdrawn. Then 8 of the animals received an injection into the basal cistern of 0·5 ml. of undiluted tissue-culture fluid containing the virus, 4 being thus injected with Type-6 virus and 4 with Type 16. An intraspinal injection of 0·1 ml. of the fluid containing the respective virus type was also given to 2 monkeys in each group. The remaining 2 control animals were injected with heated virus, Type 6 or 16, only.

In 6 monkeys (3 Type 6, 3 Type 16) signs of muscular weakness of the limbs developed, the onset being 4 to 6 days after injection. Pleocytosis could be demonstrated at the 2nd day and lasted in some instances for 21 days after injection; at the peak the C.S.F. contained 64 to 598 cells per c.mm. Type-6 virus was isolated from the blood (2nd day) and C.S.F. (2nd and 4th days) of the 4 monkeys injected with this type; Type-16 virus was recovered from the C.S.F. (2nd day) of 3 of the 4 monkeys injected with this type, but was not isolated from the blood. Virus was not isolated at necropsy from faeces or tissues. Homologous neutralizing antibody, undetectable at the time of injection, showed significant increases in titre.

The monkeys were killed 6 to 21 days after injection. Slight round-cell infiltration of the meninges was observed,

but there was no convincing evidence of neuronal damage in the spinal cord. None of these reactions was observed in the control monkeys inoculated with heated virus.

Joyce Wright

296. **The Incidence and Significance of the Leukemoid Reaction in Patients Hospitalized with Pertussis**

J. D. WELSH, W. F. DENNY, and R. M. BIRD. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **52**, 643–649, June, 1959. 1 fig., 19 refs.

A high leucocyte count is a cardinal feature of whooping-cough, and when it is in excess of 50,000 per c.mm. (leukaemoid reaction) it has, according to some authorities, been associated with an increase in the number of complications and in mortality. To determine whether the leukaemoid reaction is of prognostic significance the authors have compared two groups of patients treated at the University of Oklahoma Hospital, Oklahoma City, at different times, as follows: (1) 47 randomly selected cases seen in the period 1933–43, and (2) 127 consecutive cases admitted between 1951 and 1956. These groups were comparable in the important respects of age (range 1 month to 14 years), duration of disease on admission (average 2 weeks), and proportion of severely ill patients; and when the groups were subdivided on the basis of the presence or absence of a leukaemoid reaction there was no significant difference in age, sex, or duration of symptoms.

A leukaemoid reaction was recorded in 30% of cases in Group 1 and in 19% of those in Group 2, a difference stated to be not statistically significant. Among these the incidence of complications was about the same in the two groups and the mortality was not significantly different. There was, of course, with modern treatment a significant decrease in complications and mortality in the patients seen in 1951–6, but this improvement occurred almost exclusively in those who did not exhibit a leukaemoid reaction. It is inferred that such a reaction in a patient with whooping-cough is an adverse factor in prognosis, and that this applies even more so today than formerly. *H. Stanley Banks*

297. **Clinical Characteristics of Leptospirosis. Observations Based on a Study of Twelve Sporadic Cases**

G. A. EDWARDS. *American Journal of Medicine* [*Amer. J. Med.*] **27**, 4–17, July, 1959. 8 figs., 29 refs.

The author reports a clinical study of 12 sporadic cases of leptospirosis observed at the Veterans Administration Hospital, McKinney, Texas. From these 12 patients no fewer than 5 different strains of *Leptospira* were identified serologically: *L. pomona*, *L. canicola*, *L. autumnalis* A.B., *L. grippotyphosa*, and *L. icterohaemorrhagiae*, yet all produced the same mild disease.

The clinical manifestations showed the disease to be an acute, self-limiting, diphasic illness with a low incidence of jaundice and significant renal damage. It falls naturally into two stages; the first stage is compatible with the presence of leptospiraemia seen during the initial 5 to 7 days and is followed by a second stage in which the symptoms seem to be the consequence of the body's immunological response. The author states that " the diagnosis of leptospirosis should be considered in any patient with an acute illness characterized by headache, myalgia, fever, chills and conjunctival suffusion, and in any patient in whom ' aseptic meningitis ' develops following an acute febrile illness of 5 to 7 days' duration ". The most common mode of infection is through contact with stagnant water frequented by animals or by direct contact with the urine of infected farm animals.

Edward Hindle

298. **The Treatment of Pinworm Infections in Humans (Enterobiasis) with Pyrvinium Chloride and Pyrvinium Pamoate**

J. W. BECK, D. SAAVEDRA, G. J. ANTELL, and B. TEJEIRO. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **8**, 349–352, May [received July], 1959. 4 refs.

Pyrvinium chloride and pyrvinium pamoate, soluble and relatively insoluble salts of a cyanine dye, 6-dimethylamino-2-[2-(2:5-dimethyl-1-phenyl-3-pyrryl)vinyl]-1-methylquirolinium, were tried in the treatment of infection with *Enterobius vermicularis* in white and negro children in two institutions at respectively Miami and Kendall, Florida. Both drugs were given in a dosage of 2 mg. per kg. body weight daily for 7 consecutive days. In addition, pyrvinium pamoate was given in a single dose of 5 mg. per kg. body weight. In preliminary toxicity tests mice given the chloride in a dosage of 4 to 6 mg. per kg. body weight " showed slight depression in one hour but a return to normal thereafter "; a similar reaction occurred with a dosage of 8 to 10 mg. per kg. body weight, but 3 of the animals died. The pamoate was much less toxic; in a dosage of 50 to 125 mg. per kg. body weight there was " a slight depression " in mice but no other reactions were noted with a dosage up to 300 mg. per kg. body weight. In rats given pyrvinium chloride in a dosage of 14 mg. per kg. body weight daily for 1 to 4 weeks weight gain was severely depressed; in rats given 198 mg. of the pamoate per kg. body weight daily for 2 to 4 weeks weight gains were also severely depressed. No significant blood changes were observed with either drug.

A group of 63 children received the chloride in a dosage of 2 mg. per kg. body weight, while another group of 34 received the pamoate in a dosage of 2 mg. per kg. body weight, 3 times a day for 7 days. Cure, as assessed by adhesive-tape perianal swabs taken for 30 days subsequent to treatment, was obtained in all cases. Of 14 untreated infected controls, 4 showed spontaneous cure, and of 86 untreated controls without infection, 7 had positive perianal swabs before the end of the study. Of 33 negative controls treated with pyrvinium chloride, none became positive.

A single dose of 5 mg. of pyrvinium pamoate per kg. body weight was given to 100 children with pinworm infection; 45 were negative one day after treatment, 96 being negative 8 to 14 days afterwards.

Pyrvinium chloride was not well received by the children because of its bitter taste, and nausea and vomiting occurred on several occasions. The pamoate was well received and there were no complaints of side-effects.

O. D. Standen

Tuberculosis

299. **Bronchial Abnormalities after Primary Tuberculosis**

L. E. Hill and J. E. G. Pearson. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **53**, 278–295, July, 1959. 3 figs., 45 refs.

The incidence of bronchial abnormalities after primary tuberculosis was studied at Frenchay Hospital, Bristol, in two groups of patients: (1) 71 children (out of a total of 176 treated for primary tuberculosis between 1948 and 1954) in whom there was evidence of pulmonary collapse and sufficient time had elapsed since the primary infection for bronchography to be of value; and (2) a group of 562 patients with bronchiectasis, the object being to determine the number of patients in whom this disease was attributable to antecedent primary tuberculous infection.

It was found that in 29 of the children who had had a primary infection associated with collapse bronchiectasis had developed. As expected, the longer the collapse continued and the younger the child, the greater was the risk of bronchiectasis. Although opinions differ on the exact pathological changes in epituberculosis, the authors consider that bronchial block by the diseased lymph nodes is the essential factor in the production of bronchiectasis. When bronchiectasis does develop it is commoner in the right upper and middle lobes than elsewhere and is frequently symptomless—at least in the first decades. They state that in at least 2·1% of children who contract primary tuberculosis bronchiectasis develops, this incidence being similar to that following whooping-cough, and that in at least 5·9% of all patients with bronchiectasis the cause is a previous primary tuberculous infection. They do not consider that surgery is justified in primary tuberculosis with collapse; they favour repeated bronchoscopic aspiration, although they admit that this procedure has limitations, especially in very young children.

[This is a well balanced paper containing much valuable and interesting statistical information.]

Paul B. Woolley

300. **An Experiment in Mass Radiography**

J. B. Cochran, W. B. Fletcher, and C. Clayson. *British Medical Journal* [*Brit. med. J.*] **2**, 1–5, July 4, 1959. 5 figs., 5 refs.

Between March and July, 1957, a chest x-ray survey was carried out in Dumfries designed to determine: (1) the influence of a preliminary census and of home visiting on the population response to mass radiography, and (2) the incidence of pulmonary tuberculosis in the town compared with that in a nearby rural area where a survey was carried out in 1956. The town was divided into three sectors: the first was subjected to a census together with home visiting and general propaganda, the second to a census together with general propaganda, and the third to general propaganda only. In the first sector about 88% of the population responded to the invitation to undergo x-ray examination, whereas in the second and third sectors approximately 64% responded. Home visiting increased the response by approximately 20% in the middle-aged groups and by about 30% to 40% in older age groups. A special study of those who did not attend for x-ray examination revealed that fear of the disease was the predominant factor. Active tuberculosis was found in 1·5 per 1,000 of the individuals examined; this incidence and the age and sex distribution were similar to those found the previous year in the nearby rural area.

T. M. Pollock

301. **Studies on the Effect of Isoniazid upon the Antituberculous Immunity Induced by BCG Vaccination**

M. Toyohara, S. Kudoh, and Y. Obayashi. *Tubercle* [*Tubercle* (*Lond.*)] **40**, 184–191, June [received Aug.], 1959. 4 figs., 5 refs.

In the study here reported from the Research Institute, Japan Anti-Tuberculous Association, Tokyo, which was designed to investigate whether or not live B.C.G. organisms are essential for antituberculous immunity, six groups each consisting of 9 to 12 guinea-pigs were treated as follows: (1) with isoniazid (5 mg. daily by subcutaneous injection) for 5 days before and 4 weeks after vaccination with heat-killed B.C.G. and challenged with virulent tubercle bacilli at the 5th week; (2) as in Group 1, except that the vaccination was with live B.C.G.; (3) animals in this group were not vaccinated, but were challenged at the 5th week; (4) vaccinated with live B.C.G., given isoniazid from the 2nd to the 4th week after vaccination, and challenged at the 7th week; (5) vaccinated with live B.C.G. and challenged at the 2nd week; (6) as in Group 5, but challenged at the 7th week. All animals were repeatedly tested for tuberculin sensitivity with 1 mg. of old tuberculin and were killed 7 weeks after the challenge dose. They were examined for evidence of tuberculosis, such disease in the lymph nodes and viscera being assessed roughly according to the size of the nodes or number of tubercles visible.

Animals in Group 3 had advanced generalized tuberculosis. Those in Groups 1 and 2 also showed advanced disease, though this was less severe than in Group 3. Those in Group 5 showed infection of a moderate degree, while in Groups 4 and 6 the disease was slight, being very slightly more severe in Group 4 than in Group 6. The degree of tuberculin sensitivity was significantly weaker in Group 1 than in the other groups, from which it is concluded that the administration of isoniazid definitely weakened the tuberculin sensitivity produced by B.C.G. vaccination. On the basis of the over-all results it is considered that multiplication of the bacilli in the host plays an important part in the acquisition of antituberculous immunity.

John M. Talbot

RESPIRATORY TUBERCULOSIS

302. **Bronchoscopic Findings in Children and Adolescents with Pleural Effusion.** (Bronchoskopische Befunde bei Kindern und Jugendlichen mit Pleuritis exsudativa)
H. DOESEL. *Tuberkulosearzt [Tuberk.-Arzt]* **13**, 453–459, July, 1959. 2 figs., 26 refs.

Bronchoscopy was performed under general anaesthesia [at the Children's Sanatorium, Wangen in Allgäu, Germany] on 100 children and adolescents who had developed exudative pleurisy in the course of primary pulmonary tuberculosis. It was found that the pleurisy in its early stages was always accompanied by inflammation of the bronchial mucosa on the affected side. In some cases the mucosa of the contralateral side was also involved, although to a lesser extent. The inflammatory reaction was most pronounced in those bronchi which were in open communication with, or were compressed by, caseating lymph nodes and in those draining secondary foci. Histological examination of biopsy specimens revealed in most cases chronic inflammatory infiltration in the subepithelial tissue, with a preponderance of lymphocytes, histiocytes, and plasma cells. Chronic atrophic bronchitis was present in 9 cases. In 25 erosion of the bronchus by caseating lymph nodes with fistula formation occurred during the period of exudative pleurisy. The sputum was positive for tubercle bacilli in 18 cases, in 8 of which bronchoscopic evidence of a fistula was found. Scars of healed fistulae, already pigmented with carbon particles, were present in 6 cases. Both fistulae and scars were found more often on the right side than on the left in the proportion of 23:11. Signs of compression of the bronchus by enlarged lymph nodes were found in 13 cases and constriction due to scar formation was found in 3 others. It is emphasized that bronchoscopic changes in cases of exudative pleurisy are associated with a primary infection, and the indications for bronchoscopy are discussed.—[From the author's summary.]

303. **The Incidence of Segmental Lesions in Primary Tuberculosis in Childhood, with Special Reference to the Effect of Chemotherapy**
G. LORRIMAN and F. J. BENTLEY. *American Review of Tuberculosis and Pulmonary Diseases [Amer. Rev. Tuberc.]* **79**, 756–763, June, 1959. 19 refs.

The history of 107 children with enlarged hilar lymph nodes or a primary tuberculous complex was studied with special reference to the onset of segmental lesions. All these children, who were under 5 years of age on admission, had been discharged from High Wood Hospital, Brentwood, Essex, between 1952 and 1957. Segmental lesions developed in 26 (24%) of the children. Six of these cases were discarded for various reasons; of the 20 remaining, 10 occurred among the 41 cases given antibiotic treatment and 10 among the 50 untreated cases. (The final analysis was based on 91 of the 107 cases.) Of patients under 2 years old, 7 (44%) of 16 treated with isoniazid developed segmental lesions compared with 2 (20%) of 10 given no chemotherapy. Among children aged between 2 and 5 years segmental lesions occurred in 2 (12·5%) of 16 treated and in 8 (20%) of 40 untreated patients.

The authors stress that any conclusions they arrive at can be only tentative owing to the small number of patients. Even if the results suggest a high proportion of segmental lesions in tuberculous children under 2 years of age receiving chemotherapy, they consider that this treatment should be given for its valuable action in preventing haematogenous spread of the disease.

G. M. Little

304. **Hepatic Toxicity of Pyrazinamide Used with Isoniazid in Tuberculous Patients**
A UNITED STATES PUBLIC HEALTH SERVICE TUBERCULOSIS THERAPY TRIAL. *American Review of Respiratory Diseases [Amer. Rev. resp. Dis.]* **80**, 371–387, Sept., 1959. 2 figs., 17 refs.

Twenty hospitals participating in the United States Public Health Service Tuberculosis Therapy Trials undertook a controlled investigation of the hepatic toxicity of pyrazinamide on 780 patients with far advanced pulmonary tuberculosis. Patients were randomly assigned to 5 regimens: the control regimen, PAS with isoniazid, and 4 regimens using pyrazinamide with isoniazid. Pyrazinamide was used in two dosages, 25 and 40 mg. per kg., and each dosage was studied in both 12- and 24-week courses.

Only one hepatic episode was observed among patients receiving isoniazid plus PAS. Twelve weeks of treatment with either 25- or 40-mg. per kg. doses of pyrazinamide produced hepatic damage in 2 to 3% of the patients. With the 25 mg. per kg. dose, the rate on the 24-week course was no higher than on the 12-week course, but continued use of the 40-mg. per kg. dose for 24 weeks sharply increased the rate of hepatic toxicity to more than 6%. Although it seems unlikely that pyrazinamide's hepatic toxicity occurred at random, predisposing or precipitating factors were not detected.

The results of liver function tests before and during treatment on all regimens indicated that: (1) in tuberculous patients there was a wide range of "normal" values on serum bilirubin, bromsulphalein, and cephalin flocculation tests; (2) consequently a single high test value was less important than increase from previous levels in presaging hepatic disturbance; and (3) there was no general tendency for test values to increase during treatment with pyrazinamide.—[Authors' summary.]

305. **Relapse of Pulmonary Tuberculosis after Treatment with Antibiotics and Intrapleural Pneumothorax.** (Recidive dopo trattamento chemio-antibiotico e pneumotorace intrapleurico)
M. LUCCHESI, M. ZUBIANI, and L. CATACCHIO. *Lotta contro la tubercolosi [Lotta c. Tuberc.]* **29**, 589–618, May [received Aug.], 1959. 15 figs., 48 refs.

The authors have analysed the results in 647 patients treated for pulmonary tuberculosis at the Carlo Forlanini Institute, Rome, between 1948 and 1956, these being selected from a total of 7,980 patients on the basis of adequacy of the records and follow-up information. It was found that 70 patients (10·8%) had relapsed, this

occurring more often in men (13·79%) than in women (8·43%). Most of these patients were over 40 years of age, and 17·1% had exudative and bilateral disease as against 5·44% with unilateral disease. It is pointed out that the higher the total dosage of streptomycin, PAS, or isoniazid, especially in combination, the lower was the incidence of relapse. Relapse was commonest in the first 2 years after initial treatment and usually occurred at the original site of disease, especially in patients with cavitated disease, and was often associated with the emergence of resistance of the tubercle bacilli to the antituberculous drugs. *Arnold Pines*

306. **Relapse of Pulmonary Tuberculosis after Surgical Intervention for Collapse or Resection.** (Recidive dopo interventi chirurgici di collassoterapia e di exeresi)
N. Di Paola, P. Meoni, and G. Bertoglio. *Lotta contro la tubercolosi* [*Lotta c. Tuberc.*] **29**, 619–640, May [received Aug.], 1959. 18 figs.

The authors discuss the incidence of post-surgical relapse in 830 cases of pulmonary tuberculosis treated at the Carlo Forlanini Institute between 1953 and 1956. Of these patients, 378 were treated by thoracoplasty, 200 by the induction of extrapleural pneumothorax, and 252 by resection, partial in 174 and total (pneumonectomy) in 78.

Among the 378 subjected to thoracoplasty there was progression of the disease in 8%, but this was serious in only a small [unspecified] number of cases. Of the cases of extrapleural pneumothorax, there was progression of disease in 24·56% during treatment, but in only 1% after treatment had finished, while of the resected cases, 5·95% relapsed. The authors consider immunological factors to be important in the causation of relapse and have found the best prevention to be 1 to 2 years of chemotherapy. They also consider that collapse therapy is still an effective method of treatment, but recommend that resection be performed if there are still signs of activity of the disease after 6 months of such therapy. *Arnold Pines*

307. **Surgery in Pulmonary Tuberculosis. A Review**
R. S. Mitchell and O. Auerbach. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **80**, 207–215, Aug., 1959. Bibliography.

MILIARY TUBERCULOSIS

308. **Results of Specific Treatment of Miliary Tuberculosis in Children: a Follow-up Study of 63 Patients Treated with Antimicrobial Agents**
E. M. Lincoln and F. Hould. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 113–120, July 16, 1959. 10 refs.

The course and complications of miliary tuberculosis in 63 children treated with antibacterial drugs at Bellevue Hospital, New York, between June, 1944, and June, 1956, are compared with those in a group (comparable in most respects except for some differences in age and race distribution) of 102 children treated between 1926 and 1944 when no chemotherapy was available. In the latter ("untreated") group the mortality was 100%, 88 of the 102 children dying within 3 months of diagnosis, 11 within one year, and the remaining 3 surviving for 15 months, 2 years, and 4 years respectively. Most of these patients died from tuberculous meningitis.

The treated group is considered in subgroups according to the type of treatment given, as follows. (1) Of 9 patients who received thiazosulphone only, this being given daily for 3 years in a dosage producing blood levels of 1 to 3 mg. per 100 ml., 6 survived and none developed meningitis. Fresh tuberculous lesions appeared up to 20 months after starting treatment in 3 of these patients and in one other 3 months after completion of the course. Late complications (11 to 12 years after diagnosis) occurred in 3 cases, 2 developing renal tuberculosis and the other chronic pulmonary tuberculosis. All 6 survivors now show a calcified primary lung complex, 5 having calcification in the splenic area and one cerebral calcification, although in this case there was never any evidence of meningitis; radiological clearing was not complete until between 32 and 44 weeks. (2) In the second subgroup, in addition to thiazosulphone 29 patients were given streptomycin, 1 g. daily for 4 months, 5 of these also receiving PAS [no dosage stated]. To the 14 patients with tuberculous meningitis streptomycin was given for 6 months, usually also intrathecally. Of the total of 29 patients, 7 died, 6 having tuberculous meningitis, while the 7th was moribund on admission. Of the 14 patients with meningitis, 7 had acute and one chronic meningitis as well as recent miliary tuberculosis on admission, the 6 others developing meningitis 1 to 3 months after diagnosis and during therapy. In 8 patients tuberculous complications developed 2 to 18 months after starting treatment. At follow-up after 7 to 12 years only one late complication, namely, phlyctenular conjunctivitis, had occurred, this appearing 4 years after diagnosis. Radiography showed less calcification than in the thiazosulphone-treated group, and chest films cleared in 7 to 28 weeks, average 13 weeks.

(3) The remaining 25 patients were treated with isoniazid [no dosage or duration stated], 24 also receiving thiazosulphone as before and 20 streptomycin in addition. Only one of these patients died, 12 days after the start of treatment. Meningitis was present in 2 patients on admission, but no other frank cases developed, although in 2 cases tubercle bacilli were found in the cerebrospinal fluid; this cleared in one case after 5 days of chemotherapy and in the other after 11 days. Tuberculous complications developed in 3 patients during the first 6 months of treatment and in one 4 months after completing the course of thiazosulphone. Recent radiography has shown that calcification in the splenic area is present in 13 patients and cortical calcification in 2 who had meningitis. The radiological appearances cleared in 5 to 23 (mean 13½) weeks. In conclusion the authors stress the importance of prompt diagnosis and early treatment of miliary tuberculosis, which should always be considered when a child has sustained fever of unknown origin not responding to treatment. They also comment on the value of isoniazid in preventing the development of meningitis. *Janet Q. Ballantine*

Venereal Diseases

309. **The Behaviour of the Treponemal Immobilization Test in Syphilitic Patients.** (Probleme über das Verhalten des Treponema-pallidum-Immobilisations-Testes an syphilitischen Kranken)
I. KÁROLYI and K. KIRÁLY. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **140**, 959–964, Aug. 29, 1959. 16 refs.

A comparative study of the treponemal immobilization (T.P.I.) test and the older serological tests for syphilis has been carried out on the serum of 5,000 patients at the State Institute for Dermatology and Venereology, Budapest. In the sera of 129 syphilitic patients, most of whom had been treated, the test results showed major discrepancies; thus (1) 77 cases were seronegative but gave a positive T.P.I. reaction, while (2) 36 cases were seropositive but negative to the T.P.I. test. The discrepancy in Group 1 is considered to be due to the more persistent production of immobilisin than of reagin. The results in the second group are more difficult to explain, but it is suggested that the production of reagin in these cases was prolonged by non-specific stimuli. In a number of syphilitic patients there was a repeatedly weak T.P.I. reaction resulting from a diminished production of immobilisin, a finding suggestive of healing of the syphilitic process. *G. W. Csonka*

310. **The Nelson Test as a Criterion of Success in Antisyphilitic Treatment.** (Der Nelson-Test als Kriterium für den Erfolg der antisyphilitischen Behandlung)
W. BERLINGHOFF and G. VOGEL. *Archiv für klinische und experimentelle Dermatologie* [*Arch. klin. exp. Derm.*] **209**, 76–96, 1959. Bibliography.

The authors, who write from the University of Jena, have examined the sera of 675 patients who had been treated for syphilis in all stages, both the standard serological tests (S.T.S.) and the treponemal immobilization (T.P.I.) test being employed. Treatment had been with arsenic and bismuth, with penicillin alone, or with a combination of these methods.

In primary and secondary syphilis the T.P.I. test reaction became negative in three-quarters of the cases. In late congenital syphilis the T.P.I. test result was negative in one-eighth of the cases, but in all other stages of syphilitic infection, except early latent syphilis, there was no evidence that therapy had any influence on the results of the T.P.I. test. In 9 cases the S.T.S. gave a positive response and the T.P.I. test a negative response. In 8 of these cases, however, it was considered that the S.T.S. response was a non-specific reaction and that these patients were therefore biological false positive reactors.

The authors conclude that the possibility of achieving a negative T.P.I. test result depends solely upon the lapse of time between infection and the institution of treatment and bears hardly any relation to the type or amount of treatment given. They recommend that antenatal prophylactic therapy should be given to a syphilitic mother in each pregnancy if the T.P.I. reaction is positive, but that it is unnecessary if the T.P.I. reaction is negative.

The paper includes an excellent review of the literature on the T.P.I. test, in the course of which the authors compare their results with those of other workers in this field. *R. D. Catterall*

311. **Evaluation of the Rapid Plasma Reagin Test in Field Operation**
W. G. SIMPSON, A. W. MATTHIS, A. HARRIS, and E. V. PRICE. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **74**, 473–477, June, 1959. 2 figs., 3 refs.

It has been suggested by Portnoy *et al.* (*Publ. Hlth Rep.* (*Wash.*), 1957, **72**, 761; *Abstr. Wld Med.*, 1958, **23**, 254) that the rapid plasma reagin (R.P.R.) test is particularly suitable for use in the detection of syphilis among a shifting population. Under the auspices of the U.S. Public Health Service a large-scale field operation was therefore instituted at the Reception Center at El Centro, California, where during the period April 16 to June 28, 1957, 47,579 temporary agricultural workers (*braceros*) entered the U.S.A. from Mexico. Of the samples of serum taken from each of these workers 3,913 (8·2%) were reactive and 685 (1·4%) were weakly reactive. Clinical and dark-field microscopical examination revealed 31 cases of primary and secondary syphilis (of which 25 were seronegative), 985 of early latent syphilis, and 2,712 cases of other stages of syphilis. Of the other reactive specimens, 72 were from cases of pinta and 8 from adequately treated cases of syphilis, while in 130 cases the worker could not be located.

In order to evaluate the performance of the R.P.R. test 1,672 samples of blood previously taken from a comparable group of *braceros* were sent to the Venereal Disease Research Laboratory, Chamblee, Georgia, where they were subjected to four standard tests for syphilis; the results are tabulated for comparison. Of these specimens 45·8% were found to be non-reactive, 6·3% weakly reactive, and 47·9% fully reactive by the R.P.R. test. These results showed complete or nearly complete agreement with those of the Kolmer cardiolipin complement-fixation reaction and 94·1% agreement with the Hinton flocculation test, while 88·9% of the sera gave comparable results with the V.D.R.L. slide test, but the *Treponema pallidum* complement-fixation (T.P.C.F.) test showed only 81·4% agreement; also the last-named test showed some reactivity in 3 out of 10 specimens which were non-reactive to the other tests. It was estimated that if these other serological tests had been used at the border reception centre positive reactions would have been obtained in 3,865 by the V.D.R.L. slide test, in 4,547 by the Hinton test, in 4,948 by the Kolmer test, and in 17,452 by the T.P.C.F. test, as against the 4,598 positive reactions obtained with the R.P.R. test. *Benjamin Schwartz*

Tropical Medicine

312. **A Study of the Epidemiology of Tuberculosis in a Village Community in South India**

J. FRIMODT-MOLLER. *Indian Journal of Tuberculosis* [*Indian J. Tuberc.*] **6**, 84–95, June [received Aug.], 1959. 6 figs.

Although tuberculin testing has been extensively carried out in India in connexion with the B.C.G. vaccination campaign and mass miniature radiographic surveys have been made in various areas, little information on the attack rate and mortality from tuberculosis in the villages is available. In this paper from the Union Mission Sanatorium, Arogyavaram, the author describes a follow-up study carried out in 194 villages within 10 miles (16 km.) of the town of Madanapalle between 1950 and 1955, during which time tuberculin testing and miniature radiography of the population were carried out 4 times. Most patients in whom open tuberculosis was discovered were admitted to a special isolation hospital and treated until bacteriologically negative. The village population was 36,700 in 1950 and 39,170 in 1951, but as a result of births, deaths, and movements of the population a total of 47,814 individuals were included in the survey at one time or another. The proportion of the population under 15 years of age was 40% (compared with 27% in the U.S.A.) and 28% were over 34 (U.S.A. 42%). The reaction to the Mantoux test with 100 units of tuberculin was positive in 95% of cases. In the author's opinion " the great bulk of these reactions are caused by infection with some other microbe than the tubercle bacillus ". [No evidence is given in support of this repeated statement, and no information provided as to whether B.C.G. has been used in the area.]

In the first survey 66% of the population over 5 years old were radiographed, and by the end of the fourth 83% had been x-rayed at least once, involving 63,261 radiographs of 31, 889 persons. In the first survey 2·5% were found to be tuberculous, 40% of these cases being " clinically insignificant ", 45% " potentially active ", and 17% " active or probably active ", including 0·23% bacteriologically positive. The prevalence of active tuberculosis among males of all ages was about double that among females at the first survey, but the annual incidence of fresh cases of active disease discovered in males in subsequent surveys exceeded that for females only in the age group 30 to 49 years. The total incidence of fresh cases among persons whose first x-ray was negative was 4·14 per thousand per annum. Of these, 11% were active, 48% " observation cases ", and 41% " clinically insignificant ". Although fresh active cases occurred only in persons with a highly positive Mantoux reaction, the number of such persons in the population is so great that to give them chemoprophylaxis is impracticable. On the other hand about half of the new cases of active disease each year occurred amongst the 500-odd persons who had been kept under observation for " potentially active " or " clinically insignificant " lesions discovered previously, and most of these new cases would have been prevented by chemoprophylaxis.

Mortality from tuberculosis per 100,000, estimated to be not less than 200 in 1948–9, was 64, 46, and 21 respectively for the three intervals between the four radiological surveys. The total prevalence of the disease did not decrease significantly between 1950 and 1955, but there was a diminution in number of active cases in the younger age groups which was balanced by an increase in the older groups.

[It is nearly 5 years since the last of the surveys covered by this report. It is to be hoped that the results of more recent work will be made available soon.]

K. W. Todd

313. **Relapses after Sulfone Therapy in Leprosy of the Lepromatous Type**

J. N. RODRIGUEZ. *International Journal of Leprosy* [*Int. J. Leprosy*] **26**, 305–312, Oct.–Dec., 1958 [received Aug., 1959].

The author, working in the Department of Health, Manila, has attempted to estimate the relapse rate following sulphone therapy of leprosy in the Philippines. In the leprosaria patients are generally examined every 3 months and may be discharged at the end of a year if the results of bacteriological and clinical examination are consistently negative, but most patients prefer to remain in the leprosaria until the results have been negative for 2 years. He states that patients seek treatment chiefly to prevent blindness and deformity and not to be cured which would lead to their discharge from the leprosarium.

The sulphone drugs were introduced into the Philippines in 1946 and are now given in all cases of leprosy. At Culion Sanitarium there were 6 (1·9%) relapses in 303 cases which had been negative for 2 years, 16 (13%) relapses in 120 cases negative for 6 to 24 months, and 3 (7%) relapses in 43 cases negative for less than 6 months. Over an observation period of 3½ years (1955–8) the average relapse rate was 4·8%. Of a total of 32 relapsed cases since 1953, only 3 had received adequate treatment. In Central Luzon Sanitarium, where 96% of the 2,100 patients admitted between 1955 and 1958 were voluntary, treatment was more adequate. Over this period there was relapse in 15 cases—4 (3·9%) out of 101 cases in which bacteriological examination had been negative for 2 years, 9 (6%) out of 136 negative for 6 to 24 months, and 2 (3%) out of 67 negative less than 6 months. In Eversley Childs Sanitarium, with 1,074 inmates, treatment was most efficient; only 3 relapses were recorded after 1955—one case in which bacteriological findings were negative for 11 months, one negative for 15 months, and one negative for 26 months. At 3 other institutions with a total of 1,382 patients the results of bacteriological and clinical examination were negative in 80, of whom 3 have relapsed since 1955.

The relapse rate was also studied in 101 patients discharged from various leprosaria and given treatment at mobile clinics. There were 3 relapses after negative periods of 24 to 120 months. The author compares these figures with the relapse rate of 30 to 40% after a negative period of 5 years and a relapse rate of 75% after 10 years following treatment with chaulmoogra. He states that the results with the sulphones are obviously superior, but considers that further research on a wider scale is needed to determine how many relapses occur among those who do not continue treatment after discharge. *William Hughes*

314. **Human Trypanosomiasis in Northern Ghana 1950–56. An Epidemiological Review**
D. SCOTT. *West African Medical Journal* [*W. Afr. med. J.*] 8, 165–184, Oct., 1959. 13 refs.

315. **The Pathology and Pathogenesis of the Hepatosplenic Disease Associated with Schistosomiasis ("Egyptian Splenomegaly")**
P. K. HAMILTON, H. S. HUTCHISON, P. W. JAMISON, and H. L. JONES JR. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] 32, 18–33, July, 1959. 17 figs., 27 refs.

Egyptian splenomegaly is probably, but not certainly, due to schistosomiasis. In this paper from the American Mission Hospital, Tante, and the U.S. Naval Medical Research Unit No. 3, Cairo, its pathogenesis is critically reviewed on the basis of material from 73 patients on whom wedge biopsy of the liver had been performed at the time of splenectomy. Fairly complete clinical data were available on 47 of these patients, but not on the remaining 26. Of the former 47 there were 5 with no direct evidence of schistosomal infection, and neither adult parasites nor ova were found in the livers of the remaining 26 patients, whose urine and stools were not examined.

The livers were classified histologically into 5 groups. "Pipestem" portal fibrosis (Group I) was seen in 26 livers (36%), and in this group ova were the most frequent (92% of sections), especially in large fibrogranulomatous portal areas, where irregular vascular channels were noted. Bile ducts were always involved in the fibrous process, and moderate focal necrosis was often seen. Coarse nodular cirrhosis (Group II) was present in 19 (26%), and although there was some portal fibrosis, the characteristic lesion was the presence of numerous irregular nodules 0·5 to 1 cm. in diameter surrounded by fibrous septa. There was a chronic peripylephlebitis, and ova were present in 74% of sections. Diffuse portal fibrosis (Group III) characterized 15 (20%) of biopsy specimens, and most of the portal areas observed were affected. There were some fibrous septa, and schistosome eggs were present in 73% of sections. Ten (14%) of the 73 patients were classified as having focal portal necrosis (Group IV); they had somewhat isolated lesions which were otherwise similar to those of Group III. Group V contained only 3 patients, 2 of whom had amyloidosis.

It is concluded that schistosomiasis is the chief cause of splenomegaly in Egypt and that recurrent episodes of treatment and reinfection may load the liver with dead ova and adult schistosomes, thereby increasing the hepatic response. The liver was possibly more susceptible to infection in the subjects studied owing to their rather deficient diet. *W. H. Horner Andrews*

316. **Mass Chemotherapy in Bilharzia in Northern Transvaal**
C. J. H. BRINK, H. P. BOTHA, H. J. COMBRINK, and F. J. ERASMUS. *South African Medical Journal* [*S. Afr. med. J.*] 33, 536–542, June 27, 1959. 3 figs., 30 refs.

A survey carried out in 1957 in the Letaba District, Northern Transvaal, revealed that of 3,356 specimens of urine from native school-children, 1,669 (49·6%) were positive for eggs of *Schistosoma haematobium*, and of 2,455 stools examined, 1,419 (57·8%) were positive for eggs of *S. mansoni*, 344 (14%) for hookworm eggs, 257 (10·5%) for *Ascaris* eggs, and 24 (0·98%) for *Taenia* eggs.

It was considered that a successful scheme for the control of schistosomiasis in the territory would call for the mass treatment of at least 50,000 individuals between 4 and 16 years of age, together with an extensive molluscacide programme, improvement of sanitation in areas with a population of 1½ million backward people, provision of pure piped water supply for all household purposes, and intensive education in hygiene. Pilot control schemes were set up in specially selected areas in 1957–8 to gauge the feasibility of a large-scale programme. These schemes included clinical evaluation of the disease, mass treatment with lucanthone hydrochloride by mouth, and control of snail vectors by treatment of rivers and streams with copper sulphate. After preliminary tests in small groups of children the main trial was carried out on 445 children infected with *S. mansoni* or *S. haematobium* at Tzaneen Native School. One-third of the group were given "miracil D compound," another one-third received "nilodin", and the remaining one-third (controls) received Blaud's (iron carbonate) pills. The total dose of lucanthone was 40 mg. per kg. body weight [days of treatment not specified] and the follow-up period extended over 9 months.

A higher cure rate was obtained in cases of infection with *S. haematobium* than in cases of *S. mansoni* infection, but the results were largely vitiated by the high probability of reinfection during the long follow-up period. Thus of 143 uninfected and untreated children, 49% became infected with *S. mansoni* and 15% with *S. haematobium* during the same 9-month period in spite of the snail-control measures adopted.

It is concluded that mass treatment carried out in this way offers no solution of the problem of schistosomiasis control in Northern Transvaal. *O. D. Standen*

317. **Clinical Trials with Bephenium Hydroxynaphthoate against *Ancylostoma duodenale* and Other Helminthic Infestations**
H. F. NAGATY and M. A. RIFAAT. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] 62, 255–258, Nov., 1959. 10 refs.

Allergy

318. **Studies on the Air Spora.** [In English]
E. D. HAMILTON. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **13**, 143–173, 1959. 11 figs., 22 refs.

From the Wright–Fleming Institute of Microbiology, London, a study is reported of the numbers and types of particles in the air, the seasonal occurrence, the time of day when they are most abundant, and the influence of meteorological conditions. A quantitative and qualitative survey was made of particles of size range 3 to 40 microns which were airborne between May and September in London and in a country district 22 miles from London, an automatic volumetric spore trap being used. A further comparison was made between data obtained in two successive years at the urban site. It is stated that particular emphasis was placed on the fungus spore component of the catch, and this, together with other organic particles such as pollen grains, algae, and insect fragments, showed a seasonal and a diurnal periodicity of occurrence in the air. *A. W. Frankland*

319. **The Effects of a Ragweed Control Program on Ragweed Pollen Counts**
E. M. COHART and R. P. KANDLE. *Journal of Allergy* [*J. Allergy*] **30**, 287–298, July–Aug., 1959. 6 figs.

A study was conducted by the Department of Health of New York City during the summer of 1956 to determine if eradication of ragweed would reduce atmospheric pollen concentrations. For this purpose chemical spraying was carried out in the Bronx, 97% of the ragweed acreage being covered, and comparisons made with three other New York boroughs not so treated. These showed the daily pollen counts in the Bronx area to be no lower than those in the other (untreated) boroughs. At the same time it was found that daily pollen counts in New York City were not significantly higher whether the prevailing winds came from land areas or from the Atlantic. The authors do not, however, consider this finding to be conclusive, it being " inconsistent with the generally accepted theory that, even in an area where ragweed is generally present, atmospheric concentrations of pollen are nonetheless materially increased by wind-borne pollen from neighbouring ragweed-bearing land areas ". *H. Herxheimer*

320. **The Effect of a Ragweed Pollen Control Program on Hay Fever**
E. M. COHART and R. P. KANDLE. *Journal of Allergy* [*J. Allergy*] **30**, 299–310, July–Aug., 1959. 5 figs., 2 refs.

As a continuation of the study described in a previous paper [see Abstract 319] the authors set out to determine whether patients with ragweed hay-fever in the borough (the Bronx) subjected to ragweed eradication would suffer from fewer or less severe symptoms than those in the three untreated boroughs of New York City. Hay-fever symptoms, graded as mild, moderate, or severe, were listed for each day by 596 patients in the four boroughs investigated. It was found that patients in the treated borough did not have a lower frequency of, or less severe, symptoms that those in the other boroughs. Patients living in Manhattan, which is practically free from ragweed but has a similar pollen count to the other boroughs, had the same frequency and severity of symptoms as the rest. In all boroughs symptoms appeared about one week before the pollen was found in the atmosphere and persisted also for one week after its disappearance at the end of the season. *H. Herxheimer*

321. **Mast Cells in Bronchial Connective Tissue of Man: Importance of Such Cells in Allergic Tissue Injury.** [In English]
G. SALVATO. *Experientia* [*Experientia* (*Basel*)] **15**, 308–309, 1959. 2 figs., 3 refs.

The author, working at the Town Hospital, Merano, has identified and counted the mast cells in biopsy material taken from the orifice of the middle-lobe bronchus. The tissue specimens were fixed in formalin and stained with acid toluidine blue. In healthy subjects 45 mast cells were found in each of 20 high-power fields. The majority of these cells appeared to be full of granules, but after the sections had been treated with hyaluronidase most were degranulated. In patients with bronchial inflammation the number of mast cells was about the same as in healthy subjects, but degranulation was more marked. In patients with a specific bronchitis treated for 10 days previously with dexamethasone by mouth in a dosage of 3 to 4·5 mg. daily the number of mast cells was greatly reduced (under 15). Finally, in patients with bronchial asthma the mast-cell count was 35 in the remission phase and under 10 in the full asthmatic attack. In the latter phase very intense degranulation and disintegration were prominent; cellular changes therefore correlated with the acuteness of the asthmatic attack. *G. B. West*

322. **On Modification of Penicillin Antigenicity**
G. H. BERRYMAN and E. W. FISHERMAN. *Journal of Allergy* [*J. Allergy*] **30**, 329–336, July–Aug., 1959. 1 fig., 10 refs.

In 2 patients sensitive to benzylpenicillin results of intradermal skin tests were positive to benzylpenicillin and phenoxymethyl penicillin, but negative to penicillamine and to " synnematin " (a penicillin with a 4-amino-4-carboxy-*n*-butyl group attached). Passive transfer tests also gave negative reactions to these two substances. It is concluded that the replacement of the cyclic benzyl or phenyl group by a straight-chain 4-amino-4-carboxy-*n*-butyl group results in the loss of cross-antigenicity. *H. Herxheimer*

Gastroenterology

323. **Lesions in Upper Portion of the Gastrointestinal Tract Associated with Intracranial Neoplasms**
J. A. SPENCER, C. G. MORLOCK, and G. P. SAYRE. *Gastroenterology* [*Gastroenterology*] **37**, 20–27, July, 1959. 24 refs.

An investigation was carried out at the Mayo Clinic to determine the relationship between intracranial neoplasia and acute lesions of the upper part of the alimentary tract such as petechiae, ecchymoses, ulcerative oesophagitis, erosions, acute ulcers, and autolysis. Of 1,625 cases in which necropsy was performed between 1946 and 1951 intracranial neoplasia was present in 274 (17%). In 666 cases no neoplasms were found and these served as absolute controls; in the remaining 685 cases there were gross intracranial lesions but no neoplasms, and this group was used for the final statistical evaluation.

Acute lesions of the upper alimentary tract were found in 148 (54%) of the 274 cases of intracranial neoplasia. There was no specific type or site of neoplasm which appeared to predispose to the formation of lesions of the alimentary tract. Whether the tumour involved brain tissue or adjacent structures did not make any difference to the incidence of alimentary lesions. Further, the presence of cerebral oedema or increased intracranial pressure did not affect the coexistence of acute alimentary lesions. Other major intracranial lesions in addition to neoplasm were found in 255 cases; examination of these tended to support the premise that the formation of acute gastro-intestinal lesions may be correlated with the onset of acute intracranial lesions.

Acute lesions of the upper alimentary tract were present in only 26% of the 666 controls. There was no evidence in this study that chronic peptic ulceration was particularly associated with intracranial disease. Statistical analysis showed that there was a highly significant correlation between the incidence of intracranial neoplasm and that of acute lesions of the upper alimentary tract. *T. J. Thomson*

324. **Intracranial Infections Causing Esophagomalacia and Gastromalacia; a Postmortem Study of Eleven Cases (V. Ulcer and Brain)**
J. B. DALGAARD. *Gastroenterology* [*Gastroenterology*] **37**, 28–34, July, 1959. 4 figs., 23 refs.

The author examined the records of 3,000 consecutive cases in which necropsy was performed at the University Institutes of Pathology at Aarhus, Denmark, and Bergen, Norway (1,500 from each), with reference to the incidence of concomitant intracranial infection and ulceration in the oesophagus, stomach, and duodenum. The series included 60 cases of intracranial infection, in 11 of which there was also acute peptic ulceration. Of the 11 patients, 5 were children, 4 were females aged 17 to 77 years, and 2 were middle-aged men. In none of the cases had peptic ulceration been suspected clinically. Perforating oesophagomalacia or gastromalacia was observed in 10 of these 11 cases. The author states that these are agonal lesions and are initiated during life. He concludes that intracranial infection is an uncommon but typical cause of neurogenic peptic ulceration. *T. J. Thomson*

325. **The Role of Benign Esophageal Obstruction in the Development of Carcinoma of the Esophagus**
R. A. JOSKE and E. B. BENEDICT. *Gastroenterology* [*Gastroenterology*] **36**, 749–755, June, 1959. 28 refs.

The authors review the relationship between carcinoma of the oesophagus and preceding benign oesophageal lesions in the light of experience at the Massachusetts General Hospital, Boston, in the 10 years 1947–56. In the U.S.A. in 1946 carcinoma of the oesophagus was responsible for 0·23% of all deaths, and review of the literature shows the incidence of carcinoma in patients with benign oesophageal lesions (except for hiatus hernia) apparently to be far in excess of this.

At the Massachusetts General Hospital 4 cases of carcinoma occurred in 19 cases of oesophageal web, 3 in 58 cases of lye stricture, 3 in 180 cases of achalasia, 1 in 18 cases of congenital stricture, and 2 in 151 cases of peptic oesophagitis. These 13 cases of carcinoma complicating benign oesophageal lesions are reviewed in detail, and in particular the authors discuss the problem of the diagnosis when carcinoma develops in such lesions. This did not present as much difficulty as might be expected, and there was little delay before the malignancy was diagnosed. In 11 of the cases significant changes in symptomatology occurred, consisting in recurrence of, or rapid increase in, dysphagia in 8 and complications in 3. The carcinoma was correctly diagnosed radiologically in 8 of the 9 cases subjected to x-ray examination, the other patient having gross mega-oesophagus containing much debris. Out of 11 cases examined with the oesophagoscope, in 7 a correct diagnosis was made on the appearance, in one multiple strictures obscured the view, and in 3 the naked-eye appearances were normal. Biopsy confirmation was obtained in 9 cases, and a positive diagnosis based on cytological study of oesophageal washings was made in 2 out of the 3 cases in which this was carried out.

Although in most of these cases the condition was diagnosed early, the results of treatment were extremely poor; 10 of the patients are known to be dead, and one is alive but has metastases.

[Unfortunately no indication is given of the number of cases included in this series only because of the development of malignancy. Such cases would increase the apparent incidence of carcinoma in previously benign oesophageal lesions.] *T. D. Kellock*

STOMACH AND DUODENUM

326. **Pyloric Ulcer with Special Reference to the Gastric Secretory Pattern**
R. W. LOPES, W. L. PALMER, and J. B. KIRSNER. *Gastroenterology* [*Gastroenterology*] **36**, 790–795, June, 1959. 4 figs., 23 refs.

This is a study of the clinical and secretory features of 60 cases of pyloric ulcer, the diagnosis being based on radiological location of the lesion. This group constituted 5·5% of all cases of peptic ulcer seen in the Department of Medicine at the University of Chicago over a 5-year period. In 10 cases studies of gastric secretion were not available. Of the remaining 50 cases, 9 were in women and are considered separately and 12 had combined lesions (duodenal deformity in 7, gastric ulcer in 3, and active duodenal ulcer in 2). The gastric secretion was estimated by aspiration of juice for one hour under basal conditions, followed by histamine stimulation (0·5 mg. per kg. body weight) and collection for a further hour. The results were compared with those previously reported (*J. Lab. clin. Med.*, 1955, **46**, 307; *Abstr. Wld Med.*, 1956, **19**, 207) in healthy subjects and in patients with gastric or duodenal ulcer. The comparison showed that the patients with pyloric ulcer had a gastric secretory pattern falling between that of patients with gastric ulcer and of those with duodenal ulcer, both men and women, before and after stimulation. The symptomatology of pyloric ulcer showed no such characteristic pattern as has been suggested by other authors. *T. D. Kellock*

327. **A Survey of Duodenal Ulcer (724 Cases)**
D. L. KIPPEN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **81**, 91–97, July 15, 1959. 14 refs.

The clinical aspects of 724 cases of duodenal ulcer seen at the Winnipeg Clinic were studied. Typical ulcer distress was described by only 60% and suggestive ulcer distress by another 25% of the series. Hyperirritability of the gastro-intestinal tract was a common complaint, involving the lower oesophagus and gastric region in 50% and the colon and rectum in 27% of cases.

The type of medical treatment varied considerably, depending on such factors as the personality of the patient and the severity of his disease. Medical treatment seemed to relieve symptoms and promote ulcer healing, but failed to reduce the incidence of recurrent attacks significantly. Anticholinergic drugs failed to provide additional benefit when added to the usual ulcer program. Complications of duodenal ulcer were haemorrhage in 19%, perforation in 7%, and obstruction in 4% of cases.

The overall incidence of operation for duodenal ulcer was 21%, there being a significant difference in the groups of patients under the care of the other internists, the author, and the surgeons. Possible reasons for this variation are discussed. The occurrence of complications and the need for ulcer surgery seemed to be determined more by the severity of ulcer disease than by the doctor in charge of the case, or the type of treatment carried out by the patient.—[Author's summary.]

LIVER AND GALL-BLADDER

328. **The Mechanism and Importance of Peripheral Ammonium Metabolism.** (Mécanisme et importance de la métabolisation périphérique de l'ammonium)
J. DE GROOTE, A. M. DAWSON, W. S. ROSENTHAL, and S. SHERLOCK. *Acta gastro-enterologica Belgica* [*Acta gastro-ent. belg.*] **22**, 323–334, June–July, 1959. 4 figs., 17 refs.

In this joint communication from the University of Louvain and the Postgraduate Medical School of London it is recalled that the ammonium ion is normally metabolized by the liver, but in patients with hepatic disease and in healthy human subjects or dogs given rapid infusions of ammonium chloride the peripheral utilization of ammonium starts as soon as the arterial ammonium concentration rises. As the authors have previously shown (*Clin. Sci.*, 1957, **16**, 413; *Abstr. Wld Med.*, 1958, **23**, 181) this peripheral mechanism can be inhibited by the administration of acetazolamide, which sometimes precipitates hepatic coma in patients with severe disease of the liver.

In view of the known metabolic role of α-ketoglutaric acid as an ammonium acceptor the authors have measured the difference in the peripheral arteriovenous concentrations of this keto-acid in patients in hepatic coma or precoma, but found that this difference was not significantly greater than that found in normal subjects, and so conclude that the peripheral ammonium uptake does not seem to involve the utilization of α-keto-acids.
P. C. Reynell

329. **Recurrent Jaundice of Pregnancy. A Clinical Study of Twenty-two Cases**
A. SVANBORG and S. OHLSSON. *American Journal of Medicine* [*Amer. J. Med.*] **27**, 40–49, July, 1959. 13 figs., 17 refs.

Further to the senior author's previous study of recurrent jaundice of pregnancy (Svanborg, *Acta obstet. gynec. scand.*, 1954, **33**, 434) the authors now report 22 additional cases of the condition seen at the University Second Medical Clinic, Gothenburg. Typically, a mild jaundice appeared some time during the last 4 months of pregnancy; the serum bilirubin level increased rapidly to between 3 and 6 mg. per 100 ml. within a week or so, but thereafter showed little variation and cleared up quickly on delivery. Itching of the skin was a common accompaniment, but there was no impairment of nutrition. The stigmata were those of obstructive jaundice, but there was no evidence of parenchymal liver damage. The serum alkaline-phosphatase level was increased and hepatic biopsy examination revealed bile thrombi in the canaliculi. The blood proconvertin–prothrombin levels fell somewhat in all cases and to a degree " threatening a predisposition to hemorrhage " in 7, but the level could readily be restored by administration of vitamin K.

The general picture resembles that of the jaundice seen as a complication of the administration of chlorpromazine or methyltestosterone. Prognosis is good even when the condition recurs in successive pregnancies,

which it usually does. The cause of the disease is not known, but the authors are satisfied that it is not of haemolytic pathogenesis. There was no evidence of a hereditary factor, although one patient reported that an elder sister had similarly developed jaundice during two pregnancies. *J. McMichael*

330. **Observations on Cirrhosis and Liver Cancer at Dakar, French West Africa**
P. E. STEINER, R. CAMAIN, and J. NETIK. *Cancer Research* [*Cancer Res.*] **19**, 567–580, July, 1959. 20 refs.

This paper from the University of Pennsylvania and the Institut Pasteur, Dakar, French West Africa, deals with careful and painstaking observations on (1) primary cancer of the liver; (2) cancer associated with cirrhosis; and (3) cirrhosis of the liver alone. The patients were all native Africans of many different tribes, and were mostly of true negro or western Hamitic race, although no doubt some were of mixed origin. The majority were believed to be Moslems, a point of importance in relation to consumption of alcohol.

Of the 238 cases of primary cancer of the liver, 84% were in males and 16% in females. The average age of these patients was only 36 years, the oldest being 64 and the youngest 13. In 94 cases cirrhosis was also present, but in 61 it was completely absent; in the remainder the records were inadequate to allow of a definite conclusion on this point. The aetiology of the cancer could not be established, but the authors were convinced that it was certainly not due to alcohol, schistosomiasis, veno-occlusive disease, or nutritional factors. It is suggested that the concomitant cirrhosis indicated the presence of a liver-injuring agent rather than being itself a carcinogenic factor.

An equal number of cases of cirrhosis (238) were investigated, of which 158 were in males and 36 in females. Of these patients, 104 also proved to have cancer and 134 had not. After careful histological examination most cases (66%) of cirrhosis were classified as of the post-necrotic type. The average age in this group was 34·6 (range 15 to 60) years. Again no positive aetiological factor could be found, but the most likely appeared to be viral infection, since acute infective hepatitis is known to occur frequently in the area around Dakar. *J. W. McNee*

331. **Portal Hypertension and Bleeding Esophageal Varices—Their Occurrence in the Absence of Both Intrahepatic and Extrahepatic Obstruction of the Portal Vein**
W. A. TINSDALE, G. KLATSKIN, and W. W. L. GLENN. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 209–218, July 30, 1959. 8 figs., 30 refs.

Over a recent 8-year period 5 cases of bleeding oesophageal varices with portal hypertension but without demonstrable intrahepatic or extrahepatic venous obstruction were seen at the Grace–New Haven Community Hospital, Connecticut, 4 being described in the present paper. No major abnormality of liver function was found in any of the cases and the liver was normal in size and consistency. In 2 cases clinical examination revealed an enlarged spleen and in all cases portal venography demonstrated a normal portal venous system except for the presence of collateral channels; there was no distortion of the intrahepatic vascular pattern. At laparotomy, which was performed on all 4 patients, the pressure in the portal vein on direct measurement ranged from 230 to 375 mm. of saline, confirming the presence of portal hypertension. After portacaval anastomosis in 2 cases and splenorenal anastomosis with splenectomy in 2 the pressure in the portal system fell to normal. The only constant hepatic histological changes were slight sinusoidal distension and slight periportal fibrosis. There was no evidence of cirrhosis.

The authors discuss similar cases of hypertension without obstruction of the portal vein which have been reported in the literature. They consider that in the absence of portal vein obstruction the cause of the hypertension may be an increased blood flow through the portal vein. This could be due to increased blood flow from organs such as the pancreas, bowel, spleen, or liver into the portal system as a result of some structural or functional derangement of the blood vessels of these viscera. In the cirrhotic liver the hepatic artery may supply a higher percentage than normal of the hepatic blood flow and may contribute significantly to portal hypertension in patients with cirrhosis. It is suggested that measurement of the portal blood flow at laparotomy in patients with portal hypertension without intrahepatic or extrahepatic obstruction might help to elucidate the non-obstructive factors producing this disorder.

A. E. Read

332. **Effect of Combined Administration of Amino-binding Substances in Hepatic Encephalopathy**
W. K. YOUNG, J. V. V. JOHNSON, H. E. TICKTIN, and J. F. FAZEKAS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **238**, 60–65, July, 1959. 14 refs.

Hepatic encephalopathy is often associated with a high blood ammonium level. In animals a combination of L-arginine and monosodium L-glutamate gives protection against ammonium toxicity. At the District of Columbia General Hospital, Washington, 11 patients with Laënnec's cirrhosis and evidence of encephalopathy were given infusions of a solution of 5% glucose in water containing 25 g. of L-arginine and 22·5 g. of monosodium L-glutamate per litre over periods ranging from 5 to 24 hours. Although there was a rise in cerebral blood flow and in cerebral oxygen consumption, normal values were not reached. There was also a temporary reduction in the arterial and cerebral venous blood ammonium levels. Only 2 of the 11 patients recovered sufficiently to leave hospital; as spontaneous recovery does occur the authors did not feel justified in attributing these results to the treatment given. In their view endogenous ammonia is not the only factor responsible for this type of encephalopathy. *R. Schneider*

333. **Corticotropin (ACTH) and Adrenal Steroids in Liver Disease: a Critical Review**
M. B. GOLDGRABER and J. B. KIRSNER. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **104**, 469–489, Sept., 1959. Bibliography.

Cardiovascular System

334. **Arterial Pressure in Men Over Sixty**
F. EDWARDS, T. MCKEOWN, and A. G. W. WHITFIELD. *Clinical Science* [*Clin. Sci.*] **18**, 289–300, May [received Sept.],1959. 1 fig., 10 refs.

Arterial pressure has been measured in 1,723 representative men over the age of 60. Mean systolic pressure increased over the age period 60 to 89. The relationship was not linear, however, for the increment decreased with consecutive 5-yearly intervals. There was no appreciable change in mean diastolic pressure over the same age period. The possible effect of differential mortality on these observations is discussed.

Mean arterial pressures were lower in men smoking cigarettes than in men not smoking, and the means were inversely related to the numbers of cigarettes smoked daily. Pressures in pipe smokers were intermediate, but were nearer to those of cigarette smokers than of men not smoking. Mean arterial pressures were higher in men who drank alcohol (spirits or beer) regularly than in those who drank irregularly or did not drink. By combining the observations on smoking and drinking it is shown that pressures were highest in men not smoking who drank regularly, and lowest in smokers who did not drink.

Arterial pressures were not consistently related to the physical or mental demands of the men's occupations. In men aged 60 to 69 pressures were higher in Social Classes IV and V (partly skilled and unskilled occupations) than in Classes I and II (professional and intermediate occupations). Among men over 70 there was no consistent relationship between pressure and social class.—[Authors' summary.]

335. **Demonstration of Muscle Sphincters as a Capillary Component in the Human Heart**
D. V. PROVENZA and S. SCHERLIS. *Circulation* [*Circulation*] **20**, 35–41, July, 1959. 8 figs., 12 refs.

Histological studies were made of the capillary bed in the human myocardium and a system of muscle sphincters is described. These sphincters occur at the junction of the metacapillary with its parent arteriole and in precapillaries at their point of attachment with the parent vessels. Both these sphincters are identical in their position and anatomical features with the muscle cells from the media of the larger vessels. Arterio-venous anastomoses were observed to occur between arterioles and venules or between metarterioles and venules. The walls of these vessels were thicker when the parent vessel was an arteriole. Nerve fibres are demonstrated to accompany the capillaries. At intervals a fibre is extruded to the muscle sphincters. The fibre there becomes splayed, and the knotted end terminates in the region of the nucleus. True capillaries do not possess these fibres, which are associated only with muscle cells, but sphinctered capillaries do. *J. B. Wilson*

336. **Pitfalls in the Electrocardiographic Diagnosis of Left Ventricular Hypertrophy: a Correlative Study of 200 Autopsied Patients**
A. H. GRIEP. *Circulation* [*Circulation*] **20**, 30–34, July, 1959. 4 refs.

The results of this study reported from Massachusetts General Hospital, Boston, in which the electrocardiographic findings were correlated with the necropsy findings in 200 cases of left ventricular hypertrophy re-emphasize the shortcomings of the scalar electrocardiogram as a means of determining the presence or absence of left ventricular hypertrophy by the use of any single criterion, or indeed of several criteria. The electrocardiogram was normal in 15% of these cases, and in only 22% were Sokolow's criteria fulfilled (that is, that the sums of SVI plus RV5 or RV6 exceed 35 mV.).

In the present series the most reliable criterion for the diagnosis of left ventricular hypertrophy was the presence of the classic ST–T change (sloping of the S–T segment with minus–plus T waves in the left ventricular leads), but this was present in only 55% of the cases. It is suggested that the fact that 51 out of the 200 cases showed a taller R wave in V6 than in V5 may be of some diagnostic importance, but this is only significant of hypertrophy in the absence of a mid-anterior myocardial infarction in which the lateral wall of the left ventricle has been spared. *William A. R. Thomson*

337. **Studies in Pericarditis. I. Differentiation of the Acute Idiopathic Form from That Occurring in Disseminated Lupus**
C. F. MCCUISTON and K. M. MOSER. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **4**, 42–55, July, 1959. Bibliography.

The authors have studied at the District of Columbia General Hospital and Georgetown University Medical Center, Washington, D.C., two series of cases of pericarditis. The first consisted of 23 cases of classic acute idiopathic pericarditis (A.I.P.) and the second of 14 cases of disseminated lupus erythematosus (D.L.E.) in which pericarditis was present at the time of admission to hospital. The relevant literature was extensively reviewed in an attempt to establish criteria by which to differentiate the two conditions.

The results are discussed under three headings: (1) the occurrence and frequency of diagnostic confusion between the two diseases; (2) their points of similarity; and (3) the features in which they differ. In the discussion the authors point out that the diagnosis of A.I.P. is a diagnosis of exclusion. All apparent cases of this condition should therefore be fully investigated and the possibility of D.L.E. being also present always borne in mind, especially if the following divergent features in favour of a diagnosis of D.L.E. are observed: antecedent upper-respiratory-tract infection, gastro-intestinal symp-

toms, hypertension, congestive heart failure, some form of skin eruption, hepato- or splenomegaly, a low leucocyte count, anaemia, and a clear-cut result in the L.E.-cell test. Only in this way can other possible causes of A.I.P. be eventually differentiated. *J. B. Wilson*

CONGENITAL HEART DISEASE

338. **Patent Ductus Arteriosus in Adult Life**
G. HAMILTON FAIRLEY and J. F. GOODWIN. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **53**, 263–277, July, 1959. 8 figs., 34 refs.

The authors discuss the problems associated with patent ductus arteriosus in adult life with reference to 43 patients over 20 admitted to St. Bartholomew's and Hammersmith Hospitals, London, during the past 10 years. Five of the 31 women were over 50, but none of the 12 men, and it is suggested that men may die sooner owing to the added effect of ischaemic heart disease on the already increased left ventricular work. Angina of effort, not previously described in this condition, was noted in 3 patients. Eisenmenger reaction with right-to-left shunt was present in 3 patients, and it is once more pointed out that surgery has little place in these cases. This group apart, however, closure of the ductus is indicated regardless of age and lack of symptoms. Operative mortality in symptomless patients is 0·5% or less. In this series there were no deaths in 36 operations for closure, despite the fact that the oldest patient was 66 at the time of operation and was in congestive failure. Pulmonary vascular resistance may continue normal for many years despite a greatly increased pulmonary blood flow. These patients may remain symptomless until middle life, but may then deteriorate rapidly. *T. Semple*

339. **Pure Ventricular Septal Defect and Ventricular Septal Defect with Pulmonic Stenosis: Hemodynamic and Clinical Changes following Open Heart Surgery**
V. MARANHAO, G. T. RABER, and H. GOLDBERG. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **4**, 155–162, Aug., 1959. 19 refs.

At the Brith Sholom Cardiopulmonary Laboratory (Hahnemann Medical College), Philadelphia, the authors have carried out a clinical evaluation and cardiac catheterization both before and after open heart surgery in order to assess the postoperative haemodynamic changes in 7 patients with ventricular septal defect (Group 1) and 5 with ventricular septal defect combined with pulmonary stenosis (Group 2) operated on by Bailey. All the patients were acyanotic except one in Group 2, and in all it was confirmed that the shunt at ventricular level had been completely eliminated at operation.

Of the patients in Group 1, the dyspnoea present in 4 preoperatively was relieved in all, while the harsh systolic murmur present in all 7 patients before operation disappeared in 2, decreased in 4, and remained unchanged in one. Following operation the right ventricular and pulmonary arterial pressures were normal or near normal in 6 cases, having fallen most markedly in those with the highest preoperative pressures; the 7th patient developed an infundibular pressure gradient, which was due to obstruction caused by suturing the free wall of the right ventricle around the septal defect. All patients showed a marked fall in effective right ventricular work. Pulmonary vascular resistance was unchanged in 2 cases, fell in one, and rose in one. In the patients in Group 2 operation resulted in a marked reduction in right ventricular pressure and in the systolic pressure gradient between the right ventricle and pulmonary artery. All the patients had decreased intensity of their systolic murmurs, while the preoperative symptoms of fatigue and/or dyspnoea were improved in all. In the patient with central cyanosis this was cured. All patients in both groups developed complete right bundle-branch block following operation. Since the common bundle and right and left branches are situated in the postero-inferior margin of the ventricular septal defect it is recommended that this area should be avoided so far as is possible when inserting sutures, as was pointed out by Kirklin *et al.* (*J. thorac. Surg.*, 1957, **33**, 45).
K. G. Lowe

340. **The Clinical Evolution of Shunt-operations for Morbus Caeruleus: Results of 150 Operations in a Long-term Follow-up**
C. A. MAHAIM, C. L. C. VAN NIEUWENHUIZEN, H. A. H. D'HEER, and F. SLOOFF. *American Heart Journal* [*Amer. Heart J.*] **58**, 13–25, July, 1959. 13 figs., 32 refs.

A study is reported of the long-term results of 150 operations for congenital cyanosis performed between 1948 and 1956 on 141 patients at St. Antonius Hospital, Utrecht. All except one of the survivors were re-examined in 1956 or 1957. Of the 141 patients, 33 (23·5%) had died. The results in the survivors, based on clinical symptoms, were excellent in 22, good in 81, and "insufficient" in 5. The authors emphasize the value of exact preoperative diagnosis. Catheterization or angiocardiography was carried out in all cases. Of the 141 patients, 113 had the tetralogy of Fallot, and the results of operation were better in these patients than in those with rarer forms of cyanotic heart disease. The risk of failure was greater in young children and adults than in adolescents. In the authors' view the optimum size of the operation shunt should range from 4 to 6 mm. in diameter. In 9 cases a second operation was performed. The Potts procedure was preferred (88 cases), but Blalock's operation [shunt procedure] was also carried out (42 cases). Brock's operation [infundibular punch resection or pulmonary valvotomy] was abandoned because of the high incidence of ventricular fibrillation and the poor results. Postoperative catheterization in a few cases subjected to Brock's operation revealed a left-to-right shunt and a raised arterial oxygen saturation.

There were 18 operative deaths, including 11 from cardiac arrest. Of 11 early postoperative deaths, 3 were due to cardiac failure from too large a shunt; of 4 late deaths, one was due to sepsis. Mortality was high in puny children and in those with anaemia. Favourable prognostic signs were absence of enlargement of the heart and postoperative change in the electrocardiogram indicating increased activity of the left ventricle.

Cardiac function was tested by continuous recording of oxygen consumption at rest and during effort. The authors state that an improvement in cardiac function may continue for many months or even years. [Details are not given, but graphs of cardiac function before and after operation in one case are reproduced.] They also state that in patients who survive the clinical, electrocardiographic, and radiological signs appear to stabilize after about 2 years, but the mortality rate may again rise after 10 to 15 years because of cardiac insufficiency. In their view the palliative procedures of Blalock, Potts, and Brock will eventually be abandoned, but at present operations with the aid of artificial circulation carry a much higher mortality and their long-term results are as yet unknown. *M. Meredith Brown*

CHRONIC VALVULAR DISEASE

341. **Valvular Surgery in the Young Patient with Rheumatic Heart Disease**

A. N. Brest, J. Uricchio, and W. Likoff. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **171**, 249–251, Sept. 19, 1959. 1 fig., 3 refs.

It has been assumed that surgery for rheumatic heart disease should be limited to older patients because of the supposed risk of reactivating the rheumatic infection by surgery in younger patients. The validity of this assumption was tested in this report on 37 patients from 12 to 20 years of age. Fifteen had mitral stenosis, 15 had mitral insufficiency, and 7 had aortic insufficiency. In each case preoperative study revealed anatomic defects correctible at a reasonable risk, and great care was taken to eliminate the possibility of significant clinical rheumatic activity. No reactivation occurred in any case. Many of the earlier operations were done by methods since found ineffective, but in the later cases the benefits have sometimes been striking. The most impressive results accrued from the relief of mitral valve obstruction. In considering the advisability of heart surgery, therefore, the criteria applied to older patients can also be applied to patients under 20 years of age.—[Editorial summary.]

342. **The Open Correction of Rheumatic Mitral Regurgitation and/or Stenosis, with Special Reference to Regurgitation Treated by Posteromedial Annuloplasty Utilizing a Pump-oxygenator**

K. A. Merendino, G. I. Thomas, J. E. Jesseph, P. W. Herron, L. C. Winterscheid, and R. R. Vetto. *Annals of Surgery* [*Ann. Surg.*] **150**, 5–22, July, 1959. 7 figs., 27 refs.

The authors of this paper from the University of Washington School of Medicine, Seattle, state that a review of the literature on the various surgical procedures used in an attempt to correct mitral regurgitation reveals considerable dissatisfaction with the results, but that recognition of the factors involved in the production of this lesion and the possibility of using the open-heart technique have given encouragement to workers in this field. The factors involved in the evolution of mitral regurgitation are primarily contraction or loss of substance of the valve leaflets and possible contraction of the chordae. Dilatation of the annulus or valve ring occurs later and exaggerates the effect of the failure of the valve cusps to come together.

The authors consider that by performing a posteromedial annuloplasty on the mitral valve the plication not only reduces the circumference of the valve ring, but prevents the upward dislocation of the whole ring which occurs as the left ventricle enlarges. The operation is carried out under perfusion through the right chest. The right femoral artery is cannulated and the venae cavae catheterized and linked to a pump oxygenator. The left atrium is opened and the regurgitant stream can be assessed with the heart still beating. Stitches are placed through the postero-medial part of the annulus and carried forward until the ring is reduced to a two-finger orifice. Special precautions are taken to avoid air embolism from the left side of the heart before closure.

This technique was employed in 4 patients with pure mitral insufficiency, one of whom died, in 4 with mixed lesions of the mitral valve with one death, and in 2 with mitral disease and aortic regurgitation, both of whom died from ventricular fibrillation.

Aortic regurgitation in perfusion is a serious matter. A 3-ml. back leak with each normal beat may well become a loss to perfusion of 700 to 800 ml. per minute. At one operation 5 litres of blood was sucked out in 5 minutes; a tie-tape around the base of the aorta is indicated in such cases. The authors conclude that this operation is satisfactory in cases of pure mitral incompetence if they can be accurately diagnosed. Cases of combined stenosis and regurgitation are more difficult to handle and the outcome is less good. As a result of their experiences they appreciate the merits of " open " surgery on the mitral valve, but would not be prepared to advocate the widespread use of this procedure in cases of pure mitral stenosis. *T. Holmes Sellors*

343. **A Clinical Study of 1,000 Consecutive Cases of Mitral Stenosis Two to Nine Years after Mitral Valvuloplasty**

L. B. Ellis, D. E. Harken, and H. Black. *Circulation* [*Circulation*] **19**, 803–820, June, 1959. 3 figs., 26 refs.

Having previously reported the results of operation in 500 cases of mitral stenosis (*Circulation*, 1955, **11**, 637; *Abstr. Wld Med.*, 1955, **18**, 386) the authors now review the accumulated results in 1,000 patients who underwent operation for mitral stenosis at the City and Peter Bent Brigham Hospitals, Boston, between 1949 and 1956. Patients operated on earlier, before the present technique of valvuloplasty was established, and also certain patients with multivalvular disease on whom only an exploratory cardiotomy was carried out were excluded from the study. The 1,000 patients were divided into the following groups according to the classification of the New York Heart Association: (I) those with no significant symptoms—there were no patients in this group; (II) those moderately handicapped (19); (III) those with significant limitation of activities mainly because of pulmonary symptoms (711); and (IV) cardiac invalids

actually in or with threatened congestive heart failure (270). In cases of pure mitral stenosis (confirmed at operation) a correct diagnosis was made preoperatively in 94% of cases in Group III and in 84% in Group IV, but in cases in which both mitral stenosis and incompetence were present a correct preoperative diagnosis was made in only 42% in Group III and 52% in Group IV.

The operative mortality for Group III was 3·1% and Group IV 23·6%; in both groups there was a significant fall in operative mortality among the more recently treated patients. In 186 patients there had been one or more previous episodes of systemic embolism. The risk of operative embolism in the last 500 patients was 2·1% in Group III and 8·0% in Group IV; the outlook in the latter group was much graver, 8 out of 10 such patients in Group IV dying compared with 1 out of 8 in Group III. A surprising observation was the frequency of embolism in patients who were in normal sinus rhythm. Of the 913 survivors, 25 had a subsequent embolism at a mean period of 4 years after operation, an incidence of 0·7% per annum on the basis of 3,600 patient-years. Taking into account the operative mortality in each group, 71% of patients in Group III have survived for 9 years after operation and 57% of those in Group IV. These figures are considerably better than the most nearly comparable medically treated series reported by Olesen in Denmark. In regard to late deaths, 95 patients have died subsequently, 76 of these from a cardiac cause. The two most important factors influencing the results were the presence and degree of mitral insufficiency and the adequacy of the valvuloplasty. The damaging effect of valvular insufficiency takes time to appear, being more obvious at 5 years after operation than it was, for example, at one year.

Nearly one-third of all patients developed symptoms in the postoperative period which could be grouped under the term "post-commissurotomy syndrome", but this development did not appear to affect the later result of the operation, nor was this affected by the finding of Aschoff bodies in the atrial appendage. From a study of 228 patients who deteriorated after showing an initial improvement for at least one year it was concluded that again the main factors were the presence of mitral incompetence and an inadequate valvuloplasty, but in addition there were some whose deterioration was related to further attacks of rheumatic fever. Although re-stenosis of the valve does occur, it is only one of several factors of importance in the deterioration of patients; a significant degree of re-stenosis is uncommon when the original valvuloplasty is adequately carried out. Myocardial factors also play a part in the deterioration of many of these patients. In assessing patients for re-operation the authors are careful to determine whether mitral insufficiency is present or not; if it is present then the deterioration is most probably not due to re-stenosis and therefore a further conventional valvuloplasty will be unlikely to be effective. *W. P. Cleland*

344. **Raymond de Vieussens on Mitral Stenosis**
C. E. KELLETT. *British Heart Journal* [*Brit. Heart J.*] **21**, 440–444, July, 1959. 1 fig., 13 refs.

345. **Radiological Study of the Pulmonary Artery and the Lungs in Mitral Stenosis.** (Étude radiologique de l'artère pulmonaire et des poumons dans le rétrécissement mitral)
P. CHICHE, A. FOURCADE, and —. VAN DEN EYNDE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **52**, 601–638, June, 1959. 33 figs., 3 refs.

An analysis is presented from the Hôpital Lariboisière, Paris, of the radiological findings in 120 patients with mitral stenosis, most of whom were investigated by cardiac catheterization and subsequently treated surgically. These cases were classified into five clinical groups based on the presence of pulmonary oedema or congestion and the severity of pulmonary arterial hypertension. The incidence of various radiological features in each group is reported.

Summing up their findings the authors conclude that severe mitral stenosis with established pulmonary hypertension leads to prominence of the main pulmonary trunk to a degree thought to be roughly parallel to the height of the pressure. Increased hilar shadows are shown to be due to venous engorgement, as are heavy vascular markings in the central lung field, and both are evidence of raised left atrial pressure. Changes in the lung fields, such as hilar clouding, the presence of ring, nodular, or reticular markings, and pleural shadows are described and illustrated. The incidence of these changes is related broadly to the severity of the mitral stenosis and its duration. *J. A. Cosh*

DISTURBANCES OF RHYTHM AND CONDUCTION

346. **Congenital Atrioventricular Dissociation Due to Complete or Advanced Atrioventricular Heart Block: Clinical and Cardiac Catheterization Findings in Twelve Children without Cardiac Malformations, Including Three Siblings**
F. S. WRIGHT, P. ADAMS, and R. C. ANDERSON. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **98**, 72–79, July, 1959. 1 fig., 17 refs.

This paper from the Department of Pediatrics of the University of Minnesota has three main objects. The first is to report that out of 28 cases of congenital atrioventricular dissociation no anatomical congenital malformation of the heart was found in 12, an observation contrary to what has been reported in the past. The authors describe the usual clinical findings in the 12 cases. On catheterization the calculated systemic blood flow was found to be lower than the values found in healthy children; on the other hand the calculated stroke volume was within the normal range.

The second object of the paper is to show that congenital atrio-ventricular dissociation may be due either to complete or to advanced atrio-ventricular heart block. The different electrocardiographic findings in the two conditions are discussed.

Thirdly, the authors point out the familial aspect of the condition. Two children in their series were siblings and another child in the same family was also affected.

They review the literature and show that this familial tendency has also been reported by other workers.

John Rendle-Short

347. **Use of a Calcium Chelating Agent (NaEDTA) in Cardiac Arrhythmias**

B. D. COHEN, N. SPRITZ, G. D. LUBASH, and A. L. RUBIN. *Circulation* [*Circulation*] **19**, 918–927, June, 1959. 7 figs., 15 refs.

In this paper from Bellevue Hospital and Cornell University Medical College, New York, the authors describe the effect of intravenous administration of 1 g. of a chelating agent, disodium ethylenediamine tetra-acetate (NaEDTA), in 13 cases of cardiac arrhythmia, the object being to produce a rapid change in the circulating calcium level and so lessen cardiac irritability without altering other serum electrolytes. In 7 cases of supraventricular arrhythmia no alteration in rhythm occurred, although a satisfactory response to intravenous administration of potassium chloride and digitalis was later obtained. In cases of ventricular arrhythmia, most of them due to digitalis intoxication, NaEDTA produced an immediate response, but potassium chloride was needed for maintenance of this normal rhythm.

J. Robertson Sinton

CORONARY DISEASE AND MYOCARDIAL INFARCTION

348. **Experience with a Special Chair-bed in the Management of Patients Suffering from Myocardial Infarction.** (Опыт расширения режима больных инфарктом миокарда с применением кровати-кресла специальной конструкции)

A. P. MATUSOVA. *Терапевтический Архив* [*Ter. Arh.*] **31**, 77–83, July, 1959. 3 figs., 8 refs.

When a patient who has suffered myocardial infarction first sits up after having lain in the horizontal position for some time there is always a moment of danger. It has been established that even in healthy persons maintenance of the horizontal position for 3 to 6 weeks frequently causes disorders in the orthostatic reflexes and decreases the tolerance to changes of position. Levine and others have recommended the early transfer of such patients from bed to an armchair. In the present author's opinion this recommendation, although sound theoretically, is dangerous in practice, since the procedure of lifting the patient from bed to chair subjects him to unnecessary psychical and physical stress. Furthermore the author considers that to move the patient to the sitting position between the 3rd and 5th days after the infarction, as recommended by Levine, might be dangerous, since lifting the upper part of the body may decrease the blood flow to the heart and thus cause further deterioration in coronary circulation. Also, sitting in an armchair for long periods is very tiring for the patient.

With these considerations in mind the author has therefore devised a convertible bed-armchair consisting of 3 independently movable parts whereby the patient's position can be changed gradually. At first his head is slightly raised and the legs are slightly lowered, the angle to which the head is raised being then gradually and progressively increased. The bed-chair is fitted with elbow supports and a removable table for meals. Some 20 patients suffering from severe myocardial infarction have so far been treated in this new bed-armchair. In the first stage of treatment the patient sat passively for periods of 10 minutes, these being later increased to periods of 15 to 20 minutes, several times a day. The patients unanimously claimed to feel better; the change into a sitting position demanded no effort whatsoever on their part, nor did it cause undesirable changes in the pulse rate, blood pressure, or electrocardiogram. The dizziness of which patients usually complain when transferred into a sitting position was absent, a fact mainly explicable by the gradualness of the change from the lying to the sitting position. The whole period of treatment usually lasted from 2 weeks to 2 months.

F. S. Freisinger

349. **Serious Complications of Peptic Ulcer after Acute Myocardial Infarction**

J. C. SHIPP, V. W. SIDEL, R. M. DONALDSON JR., and S. J. GRAY. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 222–226, July 30, 1959. 1 fig., 18 refs.

The authors describe 6 cases in which there were serious complications of peptic ulcer during the acute phase (1st to 25th day) of myocardial infarction. Perforation occurred in 4 cases (3 deaths) and haemorrhage in 2 (both fatal). A previous history of peptic ulcer was elicited in 3 cases.

Because there is evidence of a relationship between adrenocortical activity and peptic ulcer formation the urinary excretion of 17-ketosteroids, 17-hydroxycorticoids, and uropepsin was estimated in 10 consecutive patients admitted to the Peter Bent Brigham Hospital, Boston, with acute myocardial infarction. A group of 10 patients with known coronary arterial disease but without recent infarction were studied as controls. None of the 20 patients had a history of peptic ulcer. In 4 of the 10 patients with acute myocardial infarction the uropepsin excretion was abnormally increased on admission and returned to normal during convalescence. There was no increase in uropepsin excretion in the controls. The 17-ketosteroid excretion did not differ significantly in the two groups. Urinary excretion of 17-hydroxycorticoids was slightly raised in 2 patients when they were admitted to hospital, but decreased during convalescence.

The many well-known interrelations between myocardial infarction and peptic ulcer are discussed. In the authors' view it is not generally known that peptic ulcer may occur or may become complicated as a result of myocardial infarction. It is suggested that this is analogous to the appearance of active peptic ulceration in other stressful situations. Patients with myocardial infarction and past or present symptoms of peptic ulcer should be treated for peptic ulceration, and anticoagulants avoided or given with caution. The increased urinary pepsinogen excretion in 4 of the 10 patients suggested that gastric secretory activity may be increased in some cases of acute

myocardial infarction, and that the cardiac infarction itself may represent an acute ulcerogenic stimulus.

R. S. Stevens

350. **Hormonal Therapy of Angina Pectoris.** (Гормональная терапия грудной жабы)
L. G. Fomina. *Терапевтический Архив* [*Ter. Arh.*] **31**, 83–87, July, 1959. 9 refs.

The author reports the effects of treatment with testosterone propionate on a number of biochemical indices related to atherosclerosis in 50 patients suffering from chronic angina pectoris (stenocardia) and in particular its effect on the anginal pain which was the main symptom of the condition. The treatment consisted in a course of 12 to 15 injections each of 10 to 15 mg. of the hormone given every second day. In 35 out of the 50 patients a satisfactory clinical effect was achieved, attacks of angina ceasing even in severe cases in which previously glyceryl trinitrate had been required several times a day. In the other 15 cases attacks of pain persisted, but the patients were able to do without glyceryl trinitrate. The biochemical investigation revealed a rise in the lecithin:cholesterol index and a decrease in the blood cholesterol level in one-half of the cases. The author recommends the use of testosterone propionate in the treatment of angina pectoris as a method of influencing the pathogenetic factors of atherosclerosis.

F. S. Freisinger

351. **Iproniazid in Angina Pectoris: a Double-blind Study**
M. Shoshkes, E. L. Rothfeld, M. C. Becker, A. Finkelstein, C. C. Smith, and F. W. Wachtel. *Circulation* [*Circulation*] **20**, 17–24, July, 1959. 33 refs.

Iproniazid has been widely used for the relief of angina, but side-effects, especially liver damage, have been reported. To assess further the effectiveness and safety of iproniazid a double-blind trial was conducted at the Beth Israel Hospital, Newark, New Jersey, using a dose of 25 mg. in tablet form twice daily. The patients studied had typical angina of long standing, and the electrocardiogram was abnormal in all but one. They were interviewed and examined at 2-week intervals while receiving four 4-week courses of treatment, 2 of the courses with iproniazid and 2 with inert tablets. Neither the investigators nor the patients knew which tablet was being given. The study was started with 35 patients, but only 19 completed the whole trial; 3 others completed 3 out of the 4 fortnightly periods and one completed 2 periods; 12 patients who did not keep appointments or refused venepunctures were excluded. Relief of angina was classified as excellent (75 to 100% reduction in attacks of pain or number of nitroglycerin tablets needed each week), good (approximately 50% reduction), and poor (less than 25% reduction).

All but 5 of the patients received iproniazid for 2 consecutive months. In the first of these months results were " excellent " or " good " in 64% of the whole group, and in the second month in 75%. During the 2 control periods " good " or " excellent " relief was obtained by 30% and 28% respectively. Half the patients experienced side-effects, usually mild and insignificant, and one developed jaundice of doubtful cause one month after iproniazid was discontinued. In 9 of 11 patients treated later with 25 mg. daily satisfactory relief of angina was obtained.

It is concluded that iproniazid in a dose of 50 mg. daily relieves angina, and that its effect is slowly cumulative as regards both relief of angina and causation of untoward reactions.

David Phear

352. **The Effects of an Inhibitor of Cholesterol Biosynthesis, Triparanol (*MER–29*), in Subjects With and Without Coronary Artery Disease**
W. Hollander and A. Chobanian. *Boston Medical Quarterly* [*Boston med. Quart.*] **10**, 37–44, June, 1959. 4 figs., 13 refs.

" Triparanol " (MER–29; [*p*-(β-diethylaminoethoxy)-phenyl]-1-(*p*-tolyl)-2-(*p*-chlorophenyl) ethanol) has the effect of reducing the blood cholesterol level. The metabolic action of this drug was observed by the authors for 7 months in 29 women and 21 men between the ages of 24 and 76 at the Massachusetts Memorial Hospital, Boston. Most of the patients had clinical or electrocardiographic (ECG) evidence of coronary arterial disease. During the whole period of the study the patients had an unrestricted diet. For a control period of at least 2 months iproniazid, pentaerythritol tetranitrate, or a placebo was administered. Thereafter MER–29 was given in 30 cases in doses of 250 mg. 3 times daily for one to 6 months; after a further period of 4 to 6 weeks' placebo treatment MER–29 was then again given in 25 of these cases in doses of 100 to 250 mg. daily. The remaining 20 patients received 250 mg. 3 times a day for 2 months, then 250 mg. daily for a further period.

During treatment the average reduction in serum cholesterol level amounted to 48%, the level falling roughly in proportion to the pre-treatment level within 5 to 10 days of starting treatment; this fall could therefore not be a sequel of dietary changes. On withdrawal of MER–29 the serum cholesterol level increased to the control values within 2 to 6 weeks. Radioisotope studies indicated that the total body cholesterol was also substantially reduced, and it could be shown that this was mainly due to interference with the conversion of acetate into cholesterol. Body weight, blood pressure, and urinary 17-ketosteroid excretion did not change significantly. Oestrogen excretion was not determined, but no feminizing effects have been observed so far.

While iproniazid prevented anginal attacks, the ECG was never modified by it, whereas MER–29 not only reduced the tendency to anginal attacks after exercise, but also modified the ECG changes in some of the patients. These findings suggest that MER–29 may improve the adequacy of the coronary circulation. Untoward side-effects were not encountered during the period of observation.

Z. A. Leitner

353. **The Surgical Treatment of Coronary Heart Disease: a Review and Critique of the Literature**
H. Buchwald. *Diseases of the Chest* [*Dis. Chest*] **36**, 189–198, Aug., 1959. 10 refs.

354. **Clinical Evaluation of Bilateral Internal Mammary Artery Ligation as Treatment of Coronary Heart Disease**
M. BATTEZZATI, A. TAGLIAFERRO, and A. D. CATTANEO. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **4**, 180–183, Aug., 1959. 25 refs.

In the past 5 years the authors, working at the University of Parma Medical School, have performed bilateral internal mammary artery ligation on 304 unselected patients with coronary heart disease. These 207 male and 97 female patients ranged in age from 33 to 83 years. Angina pectoris was present in 151 of them, while of the remainder 143 had evidence of previous myocardial infarction and 10 of recent infarction with or without associated angina pectoris. Complicating factors were myocardial insufficiency (230 cases), hypertension (122), emphysema (45), peripheral vascular disease (25), syphilis (2), and Raynaud's disease (1).

Within 30 days of mammary arterial ligation 288 of these patients (94·8%) were improved clinically, particularly in respect of chest pain and exercise tolerance, this improvement being marked in 10·2%, good in 47%, and moderate in 37·5%. One postoperative death occurred on the 16th day, the cause being pulmonary oedema. The early clinical improvement was maintained in 274 patients (90·4%). Early electrocardiographic improvement (in relation to voltage, S–T segment, and T wave) occurred in 195 cases (64·1%), but this was not maintained in 10 cases; there was no close correlation between clinical and electrocardiographic improvement. The authors formed the clinical impression that ligation of the internal mammary arteries was more successful in those patients who had angina pectoris without infarction than in those who had previous infarction, and also in cases of ischaemia of the anterior wall of the left ventricle as opposed to those with ischaemia of the posterior wall.

K. G. Lowe

BLOOD VESSELS

355. **Critical Study of the Relation between Hypercholesterolaemia and Atherosclerosis.** (Étude critique des relations entre l'hypercholestérolémie et l'athérosclérose)
J. PIERI and M. WAHL. *Presse médicale* [*Presse méd.*] **67**, 1181–1183, June 13, 1959. 26 refs.

After a detailed discussion of the available evidence concerning the relationship between high serum cholesterol and lipoprotein levels and atherosclerosis the importance of complex amino-acids in promoting cholesterol–lipid catabolism is stressed by the authors. An amino-acid preparation designated "Complex 67–82" [apparently marketed as "solvesterol"], each ampoule of which contains alanine, 6·6 mg., glycine, 22 mg., *iso*leucine, 29 mg., valine, 34·6 mg., and serine, 7·8 mg., is regarded by the authors as a kind of "physiological generator" between the *iso*-octane chain of cholesterol and protein complexes. Moreover, they have found that it has an effect on cholesterol catabolism.

In a trial of 67–82 on 31 patients with hypercholesterolaemia they gave a course of daily intramuscular injections [presumably of one ampoule] for 5 days, repeating the course after an interval of 20 days. The results were favourable in 27 cases, with a reduction in the serum cholesterol level by 15 to 62% in 22 and by 8 to 15% in 5. In 4 cases the treatment had no beneficial effect. Details of 5 cases are given, in 4 of which the serum cholesterol level was reduced by 6%, 17%, 8%, and 23% respectively, while in one it was increased by 10%.

Z. A. Leitner

356. **A Study of the Fibrinolysin Activity in Thrombotic Diseases.** [In English]
J. RØJEL. *Acta medica Scandinavica* [*Acta med. scand.*] **164**, 81–93, 1959. 6 figs., 4 refs.

At the County and Town Hospital, Skive, Denmark, the author has studied the serum proteolytic activity in thrombotic diseases; he considers that this proteolytic activity is the same as that responsible for the fibrinolytic effect. A technique is described for determining fibrinolysin activity which has the advantage of giving an answer within 30 minutes. The principle of the method is based on an observation of Hagedorn, who demonstrated a protamine-splitting property in serum which enables the latter to decompose protamine insulin crystals. There is spontaneous activity, but the author also uses streptokinase activation. Measurement of turbidity is used to determine the time required for a fixed amount of serum to dissolve crystals from 1 ml. of insulin retard. With activation by streptokinase the time measured is that required for reduction of the turbidity of the solution by 50%. The spontaneous fibrinolytic activity is expressed as the time required by serum, without the addition of streptokinase, to bring the turbidity of the solution to a value intermediate between the basic reading and the lowest value recorded during the experimental period.

In serum from 10 patients with thrombo-embolic disease the mean activated half-life was more than twice the half-life in 15 healthy subjects. There was some increase in the spontaneous half-life in serum from the patients, but this did not reach a significant level. The prolongation of the half-life—that is, reduced activity—coincided with the onset or aggravation of the clinical condition.

A. S. Douglas

357. **The Maintenance of a Sustained Thrombolytic State in Man. I. Induction and Effects**
A. P. FLETCHER, N. ALKJAERSIG, and S. SHERRY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **38**, 1096–1110, July, 1959. 4 figs., 35 refs.

The proteolytic and fibrinolytic effects of streptokinase, produced by conversion of plasminogen to plasmin, have been studied at the Washington University School of Medicine, St. Louis, Missouri, in 50 patients with thrombo-embolic disease. The drug was given by constant intravenous infusion in a dosage ranging from 35,000 to 150,000 units per hour after an initial priming dose. The plasma concentrations of streptokinase and accelerator globulin, the plasma activity of antiplasmin, antithrombin, and glutamic oxalacetic transaminase, and the prothrombin (one- and two-stage) and urokinase lysis times were estimated.

A marked and sustained thrombolytic state was produced, with rapid reduction of plasminogen levels and a corresponding increase in plasmin concentration occurring in conjunction with a high plasma streptokinase level. Thrombolytic activity, assessed by the digestion of isotopically labelled clots and the fibrin-plate technique, was estimated at 100 to 500 μg. of fibrin lysed per ml. of plasma per hour. There was no change in the platelet count, capillary fragility, serum protein level, or serum transaminase value following administration of streptokinase. An increase in the one-stage prothrombin time was demonstrated in every patient receiving a high dose of streptokinase, and in some patients bleeding episodes occurred. This coagulation defect was attributed to the increase in plasma antithrombin activity. Administration of hydrocortisone intravenously reduced the amount of whole-blood fibrinolysis and also prevented the development of plasma antithrombin activity produced by streptokinase. Plasma taken 1 to 3 months after streptokinase therapy was found to be insensitive to the action of streptokinase, but not to that of urokinase.

In conclusion the authors state that plasma fibrinolysis should be regarded as including both thrombolytic and plasma proteolytic manifestations. Streptokinase will stimulate thrombolysis, while concurrent administration of steroids will minimize the undesirable proteolytic effects without impairing the thrombolytic action.

Gerald Sandler

358. **The Maintenance of a Sustained Thrombolytic State in Man. II. Clinical Observations on Patients with Myocardial Infarction and Other Thromboembolic Disorders**

A. P. FLETCHER, S. SHERRY, N. ALKJAERSIG, F. E. SMYRNIOTIS, and S. JICK. *Journal of Clinical Investigation* [*J. clin. Invest.*] **38**, 1111–1119, July, 1959. 1 fig., 7 refs.

At the Washington University School of Medicine, St. Louis, Missouri, the therapeutic value and the effect on infarcted tissue of a sustained thrombolytic state induced by streptokinase were studied by the double-blind technique in 45 patients with thrombo-embolic disease, including 22 suffering from acute myocardial infarction and others from pulmonary embolism, thrombophlebitis, thrombotic arterial occlusion, and acute coronary insufficiency. The drug was administered by intravenous infusion for 30 hours in a dosage sufficient to produce lysis of 100 to 500 μg. of fibrin per ml. of plasma per hour; during the infusion 8 of the patients also received hydrocortisone intravenously. All the patients with myocardial infarction made satisfactory progress initially, but one died 3 weeks later from recurrent infarction, necropsy findings suggesting that lysis of the original clot had produced the 3-week-old infarction. The subsequent progress of the remaining 21 patients over periods up to 6 months was also satisfactory; in none of them did a cardiac aneurysm or additional infarction develop. An incidental finding in this group of patients was that administration of streptokinase enhanced urokinase excretion. In the group of 23 patients with other types of thrombo-embolic disease the clinical course suggested that thrombolysis *in vivo* had been produced in some patients; there were no confirmed incidents of pulmonary embolism during treatment. Side-effects of streptokinase, which were minimal, included occasional local sensitivity reactions and slight thrombophlebitis.

The authors conclude that streptokinase can produce thrombolysis in man, that this may be of therapeutic value in thrombo-embolic disease, and that there is no evidence of a resulting harmful effect on infarcted tissue.

Gerald Sandler

359. **Effect of Anticoagulants on Recanalisation**

A. TAYLOR and H. E. ESSEX. *Circulation Research* [*Circulat. Res.*] **7**, 658–660, July, 1959. 1 fig., 2 refs.

Recanalisation of an experimentally thrombosed vein in the rabbit occurs much more rapidly when the animal is receiving anticoagulant drugs of the coumarin variety. These data confirm the results of a somewhat similar study previously conducted by Wright and associates. [*Brit. J. Surg.*, 1952, **40**, 163; *Brit. med. J.*, 1953, **1**, 1021 (*Abstr. Wld Med.*, 1953, **14**, 482).]—[Authors' summary.]

HYPERTENSION

360. **Chlorothiazide—a Survey of Its Effects in Hypertensive Patients**

C. C. BARTELS, J. A. EVANS, and R. G. TOWNLEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1796–1802, Aug. 8, 1959. 4 figs., 10 refs.

A study of the hypotensive action of chlorothiazide is reported from the Lahey Clinic, Boston, Massachusetts, in which 65 patients with varying grades of hypertension took part. Before the trial was started all patients had been observed for a minimum period of 3 months. Chlorothiazide was then given, mostly in doses of 0·25 g. twice daily, for 2 to 7 months. The 23 patients who were already receiving ganglion-blocking agents continued to have these during chlorothiazide therapy. The average blood-pressure readings of 52 patients fell by more than 10% during the treatment period. Among the 23 patients previously treated with ganglion-blocking agents it was possible in 12 to discontinue these drugs when chlorothiazide was given and in 6 to reduce the dose by two-thirds or one-half. In patients who had previously undergone splanchnicectomy the mean blood pressure fell by an average of 27% during chlorothiazide therapy. In 28 of the 65 patients the serum potassium level fell below 3·5 mEq. per litre during treatment with chlorothiazide, often despite the concurrent oral administration of 2 or 3 g. of potassium chloride daily. The serum potassium level usually began to fall one week after starting chlorothiazide, but often did not reach its lowest level till after 4 to 5 weeks of treatment.

The authors are favourably impressed with the value of chlorothiazide, both when given alone and as an adjunct to other measures, in the treatment of hypertension. But they cite evidence that prolonged potassium depletion can cause pathological changes in the kidneys, and emphasize the need to watch for such lesions in patients who have suffered prolonged hypokalaemia after chlorothiazide therapy.

Bernard Isaacs

361. **The Treatment of Essential Hypertension in Out-patients by Paravertebral Procaine Block.** (Опыт лечения больных гипертонической болезнью паравертебральной новокаиновой блокадой в условиях поликлиники)
V. Ja. Prejger. *Советская Медицина* [*Sovetsk. Med.*] 23, 111–113, July, 1959.

The author describes the results of inducing ganglion block by means of injections of procaine in 26 out-patients suffering from various degrees of essential hypertension. The ages of these patients (8 male and 18 female) ranged from 31 to 70 years, 13 of them being between 41 and 50 years of age. The duration of the disease varied from 5 to 10 years, and the hypertension was in Stage I in 4 cases, in Stage II in 13, and in Stage III in 9. After the oral administration of procaine for 2 or 3 days to test for hypersensitivity 25 ml. of a 0·25% solution of the drug was injected on each side at the level of D1 to D4 in the region of the stellate ganglion. The majority of the patients (16) received 3 injections at intervals of 6 to 8 days, the course frequently being started during a period of hypertensive crisis; the others received only 1 or 2 injections.

Cases in Stages I and II showed clinical improvement 2 or 3 days after the first injection, the symptoms being relieved and the blood pressure falling. The degree of improvement was still greater after subsequent injections, and in 6 cases was maintained for over 4 months. However, only slight improvement was noted in cases in Stage III. Despite the small series treated the author concludes that the method is of value in the treatment of essential hypertension in out-patients.

Margot G. Dunlop

362. **The Application of a Monoamine-oxidase Inhibitor, 1-Phenyl-2-hydrazinopropane (JB–516), to the Treatment of Primary Hypertension**
L. Gillespie, L. L. Terry, and A. Sjoerdsma. *American Heart Journal* [*Amer. Heart J.*] **58**, 1–12, July, 1959. 6 figs., 6 refs.

At the National Heart Institute, Bethesda, Maryland, 21 patients with persistent moderate to severe hypertension were treated with a new drug—1-phenyl-2-hydrazinopropane (JB–516; "catron"). This compound is a potent monoamine oxidase inhibitor. Its introduction into therapeutics was suggested first by the involvement of monoamine oxidase in the metabolism of several endogenous physiologically active amines, including tryptamine, serotonin, dopamine, and noradrenaline; and secondly by the observation that postural hypotension frequently resulted from the clinical use of iproniazid, itself a monoamine-oxidase-inhibiting agent. In 8 of 9 hospital patients and in 10 of 12 out-patients the administration of JB–516 in daily doses of 12·5 to 50 mg. by mouth led to significant lowering of the standing blood pressure and in some cases also of the recumbent blood pressure. The fall in blood pressure began 3 to 14 days after starting treatment and disappeared one to 2 weeks after it was stopped. The action of the drug seemed to be cumulative, and the daily dose could be progressively reduced to 6·25 to 12·5 mg. None of the side-effects of ganglionic blockade occurred during treatment with JB–516, nor was tachycardia observed. This suggested that JB–516 lowered blood pressure by sympathetic blockade. In 6 patients a test measuring the endogenous conversion of serotonin to its metabolite 5-hydroxyindoleacetic acid demonstrated that monoamine oxidase was being inhibited during JB–516 therapy. In 4 of these patients, but not in the other 2, there was a concomitant fall in blood pressure.

One patient died from myocardial ischaemia and ventricular fibrillation during JB–516 therapy. One patient showed biochemical abnormalities of liver function which disappeared after withdrawal of the drug. Six patients suffered impairment of red–green colour discrimination after 3 to 23 weeks of treatment. There was a slow return to normal on withdrawing the drug, but 3 of 4 patients relapsed when treatment was restarted and 2 of these had a concomitant reduction of visual acuity.

The authors consider that more work is required to establish a relation between inhibition of monoamine oxidase and lowering of blood pressure in order to develop this possible new therapeutic approach to hypertension. They admit, however, that the visual defects observed after JB–516 could impose limitations on the use of this compound.

Bernard Isaacs

363. **Importance of Removal of a Fibromyomatous Uterus in the Prevention of Hypertensive Disease.** (Значение оперативного удаления матки при фибромиоме для профилактики гипертонии)
K. S. Raeva. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **37**, 118–120, July, 1959.

The author reports that of 100 patients with uterine fibroids, hypertension was diagnosed preoperatively in 60. It was observed to develop progressively in patients with multiple intramural fibroids and considerable distortion of the structure of uterine muscular coat, mucous membrane, blood vessels, and nerve fibres, whereas those with single subserous fibroids showed no evidence of such changes and no signs of hypertensive disease. The patients with multiple fibromyomata could be divided into two groups. In the first group, consisting of 30 patients whose blood pressure ranged between 140/110 and 160/90 mm. Hg, histological examination of sections of the body of the uterus showed extensive changes. In this group hysterectomy was followed by permanent reduction of the blood pressure to normal levels in all but 5 patients who were at the menopause. It is suggested that the hypertension in this group seemed to be due to irritation of the uterine receptors by the neoplastic tissue. The second group consisted of 20 patients in whom the blood pressure was persistently raised, ranging from 180/110 to 200/100 mm. Hg. In these cases hysterectomy was followed by only a temporary fall in the blood pressure, lasting not more than 2 to 3 months. It is considered that hypertensive disease in these cases was due to prolonged stimulation of the uterine receptors, resulting in formation of a permanent excitatory focus in the cerebral cortex. In these circumstances hysterectomy could have no permanent effect on the blood pressure.

S. W. Waydenfeld

Clinical Haematology

ANAEMIA

364 (a). **Clinical and Biological Study of 16 Cases of Acquired Haemolytic Anaemia.** (Étude clinique et biologique de seize cas d'anémie hémolytique acquise)
A. LAMACHE, M. BOUREL, M. L. CHEVREL, J. L. RICHIER, and P. LENOIR. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **35**, 1691–1701, May 18, 1959. 10 figs., bibliography.

364 (b). **The Morbid Anatomy of Acquired Haemolytic Anaemia.** (Lésions anatomo-pathologiques des anémies hémolytiques acquises)
A. LAMACHE, M. BOUREL, M. L. CHEVREL, J. L. RICHIER, and P. LENOIR. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **35**, 1702–1707, May 18, 1959. 16 figs., bibliography.

364 (c). **Visceral Siderosis in Acquired Haemolytic Anaemia.** (La sidérose viscérale des anémies hémolytiques acquises)
A. LAMACHE, M. BOUREL, M. L. CHEVREL, J. L. RICHIER, and P. LENOIR. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **35**, 1708–1717, May 18, 1959. Bibliography.

In these three papers from the Faculty of Medicine of Rennes the authors seek to distinguish a form of acquired haemolytic anaemia which is accompanied by clinical and histological evidence of widespread visceral effects. Among some 4,000 patients admitted to hospital there were 46 cases of acquired haemolytic anaemia, an incidence of 1·15%; of these, 19 showed evidence of auto-immune phenomena and 16 of them also had more widespread disease involving the skin, mucous membranes, liver, pancreas, adrenal glands, gonads, brain, and cardiovascular system. In contrast, of the other 27 cases of haemolytic anaemia which showed no evidence of auto-immunization, such involvement was observed in only 5. It is pointed out that the 16 patients with visceral involvement, of whom 6 died, had not received blood transfusion and were all over the age of 30. [The clinical and haematological features described do not appear to distinguish these 16 cases from the generality of cases of acquired haemolytic anaemia.] Attention is drawn to the occurrence in these patients of pigmentation of the skin and mucous membranes, hepatomegaly, various features suggestive of hypogonadism, and evidence of cardiovascular embarrassment, especially during haemolytic crises. The skin pigmentation, the absent or slight eosinopenia after injection of corticotrophin (ACTH), and the reduced urinary excretion of 17-ketosteroids during active haemolysis are regarded as evidence of adrenal hypofunction.

In the second paper the histological features seen in those cases which came to necropsy and in 32 liver biopsy specimens are described. The chief findings were of greatly increased deposition of pigments, including haemosiderin, and of degenerative changes, mainly fibrosis, which did not always parallel the deposition of pigments. In the third communication all these findings are discussed. Particular importance is attached to the dissociation of haemosiderosis and the other histological changes described. It is suggested that the degenerative changes in the viscera may be a direct consequence of auto-immune mechanisms analogous to those active against erythrocytes.

[The clinical and histological evidence adduced to distinguish these 16 cases from cases of acquired haemolytic anaemia in general is not convincing. It is permissible to wonder whether the 30 cases excluded from this report were studied equally closely and whether the two groups were comparable in regard to the duration of haemolysis.] *A. G. Baikie*

365. **Folic-acid Deficiency in Haemolytic Anaemia**
I. CHANARIN, J. V. DACIE, and D. L. MOLLIN. *British Journal of Haematology* [*Brit. J. Haemat.*] **5**, 245–256, July [received Sept.], 1959. 8 figs., 20 refs.

It is likely that the occurrence of megaloblastic erythropoiesis as a complication of haemolytic anaemia is less rare than the paucity of reports of previous cases would suggest. This paper describes 3 such cases seen at Hammersmith Hospital (Postgraduate Medical School of London). The first patient, a woman aged 73, had previously suffered from Addisonian pernicious anaemia, which responded to treatment with cyanocobalamin, but with the onset of symptomatic haemolytic anaemia and chronic lymphocytic leukaemia erythropoiesis again became megaloblastic in type; this patient responded well to folic acid, although cortisone was also required for the control of haemolysis. In the second patient, a woman aged 70, megaloblastic erythropoiesis was associated with idiopathic acquired haemolytic anaemia. Treatment with corticotrophin (ACTH) and adrenal steroids resulted in partial remission, but the megaloblastic erythropoiesis persisted. Subsequent treatment with folic acid was followed by a good reticulocyte response and the return of blood values to normal. In the third patient, an Arab male aged 22, the primary anaemia was severe thalassaemia and the partial megaloblastic change was adequately treated with folic acid.

In these 3 patients thorough haematological investigations showed that in every case the megaloblastic erythropoiesis was due to deficiency of folic acid, although in Cases 1 and 2 folic acid absorption was clearly normal and in Case 3 probably so. All 3 cases showed very rapid clearance from the plasma of folic acid injected intravenously. In comparative studies it was shown that in 3 cases of acquired haemolytic anaemia with normoblastic erythropoiesis the clearance rate of folic acid was almost as high as in those with megaloblastic erythropoiesis, in 3 cases of congenital haemolytic anaemia it was only a little less, in one case of acquired

haemolytic anaemia folic acid clearance was normal, while in 3 cases of paroxysmal nocturnal haemoglobinuria it was slower than normal; all these patients had normoblastic erythropoiesis. It thus appears that in haemolytic anaemia folic acid deficiency is likely to arise from the increased needs of the erythropoietic tissues. But since megaloblastic erythropoiesis is uncommon in haemolytic anaemia the appearance of frank deficiency of folic acid probably requires the presence of some other factor, such as pregnancy, an occult defect of intestinal absorption, or coexisting leukaemia. The results of the studies in the patients with normoblastic erythropoiesis suggest that even in these an unsuspected tissue deficiency of folic acid may exist. The anomalous finding in the case of paroxysmal nocturnal haemoglobinuria could not be explained. *A. G. Baikie*

366. **Five Years' Treatment of Addison's Anaemia with Purified Intrinsic Factor and Vitamin B_{12}.** [In English] A. P. SKOUBY and H. P. Ø. KRISTENSEN. *Acta medica Scandinavica* [*Acta med. scand.*] **164**, 233–239, 1959. 21 refs.

The results in pernicious anaemia of long-term administration by mouth of vitamin B_{12} (cyanocobalamin) and intrinsic factor derived from hog pyloric mucosa have usually been unsatisfactory. The defective absorption of vitamin B_{12} has been attributed to the development of a mucosal block due to the use of heterologous intrinsic factor. The present authors, working at the Gentofte Hospital, Copenhagen, used the preparation "bendogen" (GEA), which contains vitamin B_{12} in an amount equivalent to 50% of the vitamin-B_{12}-binding capacity of purified hog pyloric mucosa, in 7 patients over a period of 4 to 5½ years without haematological relapse. At the end of the test period the bone marrow was normoblastic in all 7 cases and the serum vitamin-B_{12} level was normal in 4. In 5 cases, however, a urinary excretion test with radioactive vitamin B_{12} suggested subnormal absorption of the vitamin. In 3 other patients treated with preparations containing vitamin B_{12} in amounts corresponding to 100% of the vitamin-B_{12}-binding capacity of hog pyloric mucosa the over-all results were inferior. *P. C. Reynell*

NEOPLASTIC DISEASES

367. **Acquired Hemolytic Anemia in Chronic Lymphocytic Leukemia and the Lymphomas**
R. A. KYLE, J. M. KIELY, and J. M. STICKNEY. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **104**, 61–67, July, 1959. 18 refs.

At the Mayo Clinic the records were studied of 27 patients seen between 1945 and 1957 in whom acquired haemolytic anaemia was associated with chronic lymphocytic leukaemia (16), Hodgkin's disease (7), follicular lymphoma (3), or lymphosarcoma (1). In most of the patients with leukaemia haemolytic anaemia was diagnosed late in the course of the disease, while in 9 of the 11 patients with lymphoma the presenting features were those of haemolytic anaemia. The average survival time after haemolytic anaemia was diagnosed was 7·2 years in patients with Hodgkin's disease, 1·6 year in those with follicular lymphoma and lymphosarcoma, and 1·1 year in patients with chronic lymphocytic leukaemia. The primary diseases were not especially associated with any other clinical or haematological features of the haemolytic process. The response to the Coombs test was positive in 11 out of 19 cases, but was not found to be of particular value either in diagnosis or in forecasting response to treatment. The results of treatment with corticotrophin (ACTH) or adrenocortical steroids in 28 haemolytic episodes in 16 cases were regarded as excellent in 9, fair in 15, and poor in 4. The effect of hormone therapy was not obviously related to the nature of the primary disease. Splenectomy was performed in 8 cases and was followed by complete remission of haemolysis in 3 and partial remission in one; in the remaining 4 cases the operation was without effect. In 5 patients who were not given hormone therapy or subjected to splenectomy survival was much shorter than in those who were so treated. *A. G. Baikie*

368. **The Survival of Red Cells and the Causation of Anaemia in Leukaemia**
G. R. TUDHOPE. *Scottish Medical Journal* [*Scot. med. J.*] **4**, 342–353, July–Aug., 1959. 6 figs., 41 refs.

A study of the survival of erythrocytes in 14 cases of leukaemia, including both the patients' own cells and transfused normal cells, is reported from the University of Sheffield. The survival of erythrocytes labelled with radioactive chromium (^{51}Cr) was measured, and in a case of erythroleukaemia the utilization of a tracer dose of radioactive iron (^{59}Fe) was followed by measuring the radioactivity in the erythrocytes for 10 days.

Of 5 cases of chronic myeloid leukaemia, erythrocyte survival was normal in 4 and reduced in one. Normal survival was found in one patient with erythroleukaemia and reduced survival in 2 patients with chronic lymphatic leukaemia. However, in most cases of acute leukaemia there was evidence of increased destruction of erythrocytes, but in 2 cases there was normal survival of the patient's own cells. Evidence is presented indicating that there is selective destruction of transfused normal erythrocytes in leukaemia. No relationship was found between the size of the spleen in chronic leukaemia and the degree of reduction of erythrocyte life-span. The author suggests that impairment of erythropoiesis is an important factor in the anaemia of acute and chronic leukaemia, but in many cases there is the additional factor of shortened erythrocyte survival.
I. McLean Baird

369. **The Association of Fatal Intracranial Hemorrhage and "Blastic Crisis" in Patients with Acute Leukemia**
R. D. FRITZ, C. E. FORKNER, E. J. FREIREICH, E. FREI, and L. B. THOMAS. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 59–64, July 9, 1959. 3 figs., 14 refs.

The relationship between rapidly rising numbers of abnormal leucocytes in the peripheral blood and deaths from intracranial haemorrhage in leukaemia was studied

in the case records of 100 consecutive patients with this disease admitted to the National Cancer Institute, Bethesda, Maryland, between June, 1954, and March, 1957. At the time of the study 81 of the patients had died; of these, 13 had a leucocyte count of over 300,000 per c.mm. at some time during the course of the disease, usually with over 90% " blast " cells. Of this group of 13 patients, 9 died from intracranial haemorrhage related to nodules of leukaemic cells (in some cases associated with " remnants of blood vessels ") in the white matter. These patients had not a prominent generalized bleeding diathesis and the platelet count was significantly higher than in the patients without such a high leucocyte count. Thrombocytopenia was not considered to be an important contributory cause of the very high incidence of fatal haemorrhage in this group, which was believed to be due to the rupture of blood vessels invaded by nodules of rapidly proliferating leukaemic cells. Of the remaining 68 patients, only 9 (13%) died from subdural or subarachnoid haemorrhage, usually due to a profound thrombocytopenia associated with generalized bleeding. Treatment was not significantly different in the two groups. *R. B. Thompson*

370. **The Influence of Chemotherapy on Survival in Acute Leukemia—Comparison of Cases Treated during 1954 to 1957 with Those Treated during 1947 to 1954**
A. Haut, S. J. Altman, M. M. Wintrobe, and G. E. Cartwright. *Blood* [*Blood*] **14**, 828–847, July, 1959. 6 figs., 11 refs.

In an earlier study undertaken to determine whether or not the therapeutic agents in use up to 1954 had increased the survival time of patients with acute leukaemia the authors (*Blood*, 1955, **10**, 875; *Abstr. Wld Med.*, 1956, **19**, 216) found evidence of such improvement only in the one-third of patients in whom complete, if temporary, remission was induced. In this further study from the University of Utah, Salt Lake City, they compare those earlier results in 78 cases (of which 58% were in children) with the results in 89 cases (55% in children) treated in the period 1954–7. They find a statistically significant prolongation of life in the latter series of patients, 50% of them surviving for more than 8 months after the onset of symptoms; further analysis however reveals that this improvement affected children, but not adults. They attribute this finding to the predominant occurrence in children of the acute lymphocytic type of leukaemia, which responds to treatment, whereas, the acute myelocytic leukaemia which predominates in adults is apparently uninfluenced by the therapeutic agents employed. Age *per se* did not appear to be related to survival. It was also found that a low initial leucocyte count in acute lymphocytic leukaemia was correlated with longer survival, but this was not true of acute myelocytic leukaemia: these relationships were observed in both children and adults.

In the earlier study referred to above the therapeutic substances then in use were adrenal steroids, folic acid analogues, and 6-mercaptopurine, these being employed consecutively rather than concurrently. It was also noted that most of the patients had received only two of these agents and that mercaptopurine was inadequately represented in the treatment regimens. Since 1955 all the above three agents have been used, as well as azaserine. The survival time among these recent patients who received three therapeutic agents has turned out to be better than among those who received only two forms of treatment, but further analysis does not show that the improvement in survival can be credited to the greater use of any one particular form of treatment, including that with mercaptopurine. In conclusion the authors draw particular attention to the relative inefficacy of the present treatment of acute myelocytic leukaemia and urge a more vigorous search for new chemotherapeutic agents active against this type of tumour. *A. G. Baikie*

371. **The Mechanism of the Anemia Associated with Hodgkin's Disease**
P. P. Giannopoulos and D. E. Bergsagel. *Blood* [*Blood*] **14**, 856–869, July, 1959. 2 figs., 32 refs.

The pathogenesis of the anaemia associated with Hodgkin's disease has been investigated at the University of Texas, Houston, by observing the survival of the patient's own erythrocytes labelled with radioactive chromium (^{51}Cr) and by studies of iron metabolism, including the fate of injected radioactive iron (^{59}Fe). In all of the 6 cases studied erythrocyte survival time was found to be shortened. Erythropoietic activity, as measured by the plasma iron clearance rate, was increased in all cases, but in only one patient was the activity sufficient to balance the modest increase in the rate of erythrocyte destruction.

Attention is drawn to low serum iron levels and lack of stainable iron in the bone marrow which was found in all these patients, and to the occurrence of hypochromic anaemia in some of them. In the authors' opinion these findings cannot be attributed to simple iron deficiency, since very large stores of iron were demonstrated in the liver and spleen at necropsy. It is suggested that utilization of iron by the precursors of erythrocytes in the bone marrow is not primarily affected, since injected ^{59}Fe citrate was cleared from the plasma very rapidly and appeared in newly formed erythrocytes in normal amounts. It seems likely that in the anaemia of Hodgkin's disease, as in the anaemias associated with chronic infections and rheumatoid arthritis, there is interference with the mobilization of iron from body stores, this resulting in low serum iron levels in the presence of normal or increased quantities of stored iron. An interesting difference between these types of anaemia is that in the anaemia associated with chronic infections the bone-marrow iron content is commonly increased, whereas in Hodgkin's disease no iron could be demonstrated in the marrow. *A. G. Baikie*

372. **Acute Leukemia. Skeletal Manifestations in Children and Adults**
T. F. Hilbish, B. E. Besse Jr., L. B. Lusted, M. L. Daves, L. B. Thomas, and C. A. Forkner. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **104**, 741–747, Nov., 1959. 25 figs.

Respiratory System

373. **Hypoplasia of the Pulmonary Arteries**
J. R. BELCHER, L. CAPEL, J. N. PATTINSON, and J. SMART. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] 53, 253–262, July, 1959. 8 figs., 11 refs.

In this paper from the London Chest Hospital 13 new cases of increased radiotranslucency of one lung (Macleod's syndrome) are reported. The characteristic radiological features of the syndrome are: (1) the whole of one pulmonary artery, or of one of its lobar branches, is diminished in size, the segmental arteries being also reduced in size and in number; (2) increased radiotranslucency of one lung or of one or two lobes is evident, owing to this decrease in vascularity; (3) the affected area of lung is decreased in size. Bronchograms in some cases may be normal or may show small round pooling " blobs ", moderate tubular dilatation of bronchi with poor filling of the smaller branches, or crowding of lobar bronchi with poor filling of segmental branches. Angiography reveals great reduction in the calibre of the affected artery and in the size and number of its branches. In the affected area the circulation rate is slowed. The essential functional defect is a great diminution in oxygen uptake, with variable reduction in the tidal volume of the affected area. The condition may be congenital in origin, rather like congenital absence of one pulmonary artery, or it may be acquired during the growing period. Symptoms are usually absent, but effort intolerance due to air-trapping may be present, and the condition may aggravate disease in the contralateral lung. *T. Semple*

374. **Partitional Respirometry in Cardio-pulmonary Disease**
R. J. SHEPHARD. *Thorax* [*Thorax*] 14, 153–160, June, 1959. 22 refs.

Impairment of the pulmonary uptake of inspired gases may be due to increased dead space, to impaired diffusion capacity, or to impaired pulmonary perfusion. To determine which component is defective partitional respirometry may be performed with the subject inhaling a three-gas mixture containing very low concentrations (0·03%) of ether, carbon monoxide, and acetylene from a Douglas bag. The uptake of each gas is then determined by infra-red analysis. Since the uptake of ether depends mainly on ventilation and only slightly on perfusion, that of carbon monoxide on ventilation and diffusion, and that of acetylene on perfusion and ventilation, a series of simultaneous equations can therefore be set out and the proportion of each of the three components calculated. Details of the apparatus and method were previously described (Shephard, *J. appl. Physiol.*, 1958, 13, 357). The author notes that the equipment is expensive and its use will probably for some time be limited to research centres. However, it inflicts minimal discomfort and inconvenience upon the patient and provides information obtainable by no other method.

In the present study, reported from the University of Cincinnati, the author has employed the method in the investigation of patients with congenital heart disease, emphysema, bronchitis, bronchiectasis, and pneumoconiosis, and also of 4 elderly subjects. By this technique pulmonary blood flow can be measured in cases of congenital heart disease with sufficient accuracy to make it of use as a screening procedure. Decreased diffusing capacity has been shown to be associated with pulmonary hypertension and emphysema. In the investigation of industrial diseases the pulmonary defect can be separated into its bronchial and alveolar components. Both diffusion and ventilation were decreased in the aged subjects investigated. *D. Goldman*

375. **The Forced Expiratory Volume after Exercise, Forced Inspiration, and the Valsalva and Müller Manœuvres**
L. H. CAPEL and J. SMART. *Thorax* [*Thorax*] 14, 161–165, June, 1959. 3 figs., 21 refs.

At the London Chest Hospital the authors have studied the effect of the Valsalva and Müller manœuvres on the one-second forced expiratory volume ($F.E.V._1$) in an attempt to explain the paradox that a patient with obstructive disease of the airways may ventilate his lungs at a rate greater than his maximum voluntary ventilation volume (M.V.V.) measured at rest. A total of 48 patients, of whom 30 had obstructive airway disease and 15 other pulmonary or cardiac disease, and 6 normal subjects were examined before and after exercise, the test being repeated after inhalation of adrenaline spray.

In the patients with obstructive airway disease the $F.E.V._1$ usually increased immediately after the exercise, with or without adrenaline, whereas no increase occurred in the control subjects and patients without obstruction. Likewise 31 patients with obstructive airway disease showed an increase in $F.E.V._1$ immediately after a forced inspiration following either a normal inspiration or expiration. This did not occur in the 6 healthy subjects. The authors suggest that the increase was probably due to an increase in the inspiratory rate. In all types of patients and also in the controls the $F.E.V._1$ was reduced immediately after reduction of the blood volume by performance of the Valsalva manœuvre. *D. Goldman*

376. **The Evolution and Early Results of Tracheal Fenestration**
E. E. ROCKEY, S. A. THOMPSON, and C. F. BLAZSIK. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 79, 773–779, June, 1959. 2 figs., 5 refs.

The authors recently described (*Amer. Rev. Tuberc.*, 1958, 78, 815; *Abstr. Wld Med.*, 1959, 25, 344) their operation of tracheal fenestration as a method for the therapeutic management of chronic pulmonary disease. In this paper from the Metropolitan Medical Center, New York, 17 further cases treated by means of tracheal

fenestration and repeated tracheo-bronchial aspiration are reported. Fair to good palliation was experienced by 6 patients, marked palliation by 5, a further 3 patients were " rehabilitated " to the extent that they could do without oxygen and walk fair distances without respiratory embarrassment, while " marked rehabilitation " occurred in 3 patients so that they were enabled to return to work. There was no operative mortality, but 8 of the patients subsequently died from various causes, not all pulmonary.

Of the 17 patients, one had far advanced bilateral tuberculosis, one cystic fibrosis, one advanced silico-tuberculosis, 7 emphysema with chronic suppurative bronchitis or bronchiectasis, and 7 dry emphysema with little or no cough or sputum. The authors consider that the dyspnoea in this last type of case is partly due to occlusion of the distal bronchi and bronchioles with whitish, tenacious, stringy, mucoid material which can be removed by aspiration through the tracheal fenestration, with subsequent relief of the dyspnoea.

G. M. Little

377. **Consideration of Cystic Fibrosis in Adults, with a Study of Sweat Electrolyte Values**

E. M. PETERSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **171**, 1–6, Sept. 5, 1959. 2 figs., 8 refs.

From Ohio State University College of Medicine, Columbus, the results of 313 sweat tests on 262 adult subjects are reported. In performing the test the supine patient is placed in a water-tight bag firmly closed round the neck, the environmental temperature raised to 90° F. (32·2° C.) for 70 minutes, and his sweat collected on specially prepared small cellulose sponges which are sealed against cleansed areas of skin at 4 standard sampling sites on the trunk. After recovery from the sponges the sweat is analysed for chloride content by the method of Schales and Schales and for sodium content by flame photometry. The average values of four samples are reported.

In 96 individuals regarded as a control group the sweat chloride concentration ranged from 4·1 to 68·2 mEq. (mean 33·8 mEq.) per litre, and the sodium concentration from 81·1 to 78·6 mEq. (mean 39·3 mEq.) per litre. Thus in normal subjects the chloride content never exceeded 70 mEq. per litre, whereas in 6 patients with confirmed cystic fibrosis (fibrocystic disease of the pancreas) it always exceeded 75 mEq. per litre, ranging between 78 and 145 mEq. per litre. Abnormal values (69 mEq. per litre for chloride and 79 mEq. per litre for sodium) were found in 8 out of 25 patients with cylindrical bronchiectasis, as also in 2 out of 31 patients with chronic bronchitis and bronchiectasis. It is pointed out that cystic fibrosis (which was unfortunately given the name cystic fibrosis of the pancreas), is primarily a respiratory disease, and further is not exclusively a disease of children. It produces protracted endobronchial disease, usually with additional disturbances in several exocrine organs (secretory glands). The sweat test is considered to be the most useful aid in the diagnosis and investigation of this disease.

Kenneth M. A. Perry

378. **Patterns of Disturbed Lung Function in Patients with Chronic Obstructive Vesicular Emphysema**

C. OGILVIE. *Thorax* [*Thorax*] **14**, 113–121, June, 1959. 2 figs., 14 refs.

The author presents from the London Hospital the results of a comprehensive study of pulmonary function in 19 patients with chronic emphysema. These fell into two groups—a younger group of 13 patients (average age 43 years) with a long history of recurrent bronchitis and dyspnoea, and an older group of 6 patients (average age 58 years) in whom dyspnoea was the presenting symptom and its duration only 2 or 3 years.

The two groups showed similar impairment of minute volume and vital capacity, and a similar increase in functional residual capacity, residual volume, and total lung capacity. The maximum voluntary ventilation, inspiratory and expiratory flow rates, and mixing efficiency were lower in the younger group, but the older group showed much more severe impairment of diffusing capacity, as estimated by the " breath-holding carbon monoxide method ", which is described. These findings confirm earlier post-mortem studies, which showed that long-standing chronic bronchitis may not produce permanent alveolar change to any severe degree, but that in cases of emphysema without bronchitis the alveolar changes manifest themselves in deficient diffusing of respired gases.

J. Robertson Sinton

379. **The Use of Mechanical Assistance in Treating Cardiopulmonary Diseases**

F. D. GRAY JR. and A. S. FIELD JR. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **238**, 146–152, Aug., 1959. 2 figs., 5 refs.

In the treatment of emphysema positive mouth pressure breathing tends to over-distend the already distended lungs. In order to minimize this effect the authors have tried a rhythmically operated pneumatic belt which covers the lower ribs and abdomen and is timed to inflate and deflate synchronously with a positive pressure breathing (P.P.B.) apparatus. In these cases the action of the diaphragm is often very weak, and the authors therefore employed in addition an electronic neuromuscular stimulator, of which one of the electrodes was applied to the epigastrium and the other to the lower abdomen, each receiving rhythmic stimuli alternately. Both types of apparatus were then tried on normal individuals and patients suffering from a variety of chest complaints, the aim being to assess the practicability and immediate effect on ventilation of these mechanical aids to respiration. Both types improved ventilation. In 2 patients with carbon dioxide narcosis their use in conjunction was life-saving. The effect of the apparatus is to lower the late tidal-air CO_2 concentration and increase the arterial oxygen tension. In 18 normal subjects using the neuromuscular stimulator there was an increase in tidal volume. On the whole the patients tended to " accept " the appliances better than the healthy subjects. As is pointed out, obviously the effects on the respiratory function of these patients are purely temporary, but the authors intend to investigate in a later study the prolonged use of both appliances.

Paul B. Woolley

Otorhinolaryngology

380. **Malignancies of the Paranasal Sinuses**
W. G. HEMENWAY and J. R. LINDSAY. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **70**, 61–64, July, 1959. 3 refs.

Malignant disease of the paranasal sinuses is not common. In 25 years only 62 cases have been seen at the University of Chicago Clinics, of which 56 were carcinomatous and 6 were in the "sarcoma group". Before 1948 the treatment of carcinoma was predominantly by radiation—usually deep therapy with some radium insertions—though some patients were treated by surgery, of a type now considered "conservative", followed by irradiation. Since 1948 treatment has usually been by radical surgery, either alone or followed by irradiation, and the results are certainly much better. Of 11 patients treated primarily by surgery, 6 (55%) are apparently cured after 4 to 11 years, the results being rather better when surgery was followed by irradiation. In contrast, of 8 patients treated during the same period with x rays, followed in 5 by radical surgery for recurrence, only 2 have survived, both with persistent tumour. The prognosis in adenocarcinoma is better than in squamous-cell carcinoma. For plasmocytoma and sarcoma on the other hand x-ray therapy alone appears to be very effective, 5 out of the 6 patients in this group being alive and well after 3½ to 13 years.

F. W. Watkyn-Thomas

381. **The First One Hundred Cases of Hearing Improvement in Stapes Mobilization—a Long Term Report**
S. ROSEN and M. BERGMAN. *Laryngoscope* [*Laryngoscope (St Louis)*] **69**, 1060–1065, Aug., 1959. 5 refs.

The authors present the follow-up results in 100 patients operated on by Rosen's indirect method of mobilization of the fixed stapedial footplate by exerting pressure on the neck of the stapes. Of these patients, 80 have maintained improved hearing (a gain of 15 db. or better) for periods ranging from 3 to 7 years. The remaining 20 patients showed a regression in hearing, which was complete in 16 and partial in 4. Of these 16 patients, 9 underwent further surgery, with the result that 7 of them once again acquired and have maintained improved hearing.

H. D. Brown Kelly

382. **The Perceptual Process in Speechreading**
J. B. BRANNON JR. and F. KODMAN JR. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **70**, 114–119, July, 1959. 2 figs., 12 refs.

At the Lexington Clinic, University of Kentucky, experiments were carried out on two groups, one consisting of 8 deaf subjects, average age 54·3 years, who were experienced in lip-reading, and the other of 8 normal subjects, average age 22·6 years, with no previous experience. In the Utley Sentence Test the "skilled" group obtained a mean score of 105 words out of a total of 125 (31 sentences). When asked to lip-read single, isolated words, however, there was no significant difference between the two groups, the mean score of the skilled group being 19·75% (range 14 to 30%) of 50 words and that of the unskilled 12·5% (range 6 to 22%). It is concluded that "the visibility of the total-movement form of a word is the best cue the lip-reader has in identifying it", the ease of identification of the phonetic elements of a word being dependent on whether articulation takes place at the front or back of the mouth. The superiority of the skilled lip-reader in understanding sentences lies in his recognition and use of "contextual, situational and other clues".

[The practical importance of this elaborate study is obvious. The would-be lip-reader must be encouraged to try short sentences rather than single words as soon as possible in his teaching. Another point of great importance in attempting to estimate a patient's real hearing power is that he should always be tested with single words or syllables; otherwise the test will be one of intelligence rather than deafness.]

F. W. Watkyn-Thomas

383. **Observations on Laryngeal Tumours in Females.** (Considerazioni sui tumori laringei nel sesso femminile)
B. FRANCHI. *Radioterapia, radiobiologia e fisica medica* [*Radioter. Radiobiol. Fis. med.*] **14**, 215–225, 1959.

Laryngeal tumours are much less common in females than in males, the sex ratio being between 1:5 and 1:10. Intrinsic growths, chiefly involving the vocal cords, are much more common than extrinsic growths in males, the ratio being about 20:1. In females in contrast tumours of the larynx are mostly extrinsic, that is, pharyngo-laryngeal, involving the epiglottis, ary-epiglottic folds, piriform fossa, and arytenoid cartilages. In the present paper 26 such cases treated at the Institute of Radiology of the University of Bologna during the period 1930–57 are analysed. The highest incidence was in the 5th decade (6th in the male), suggesting a possible relationship to the menopause. Histologically, the lesions were nearly all squamous-celled carcinomata, as in males. Smoking was much less prominent as a possible causative factor than in males, but a recent increase in incidence may be related to increased smoking among women.

The great majority of these patients presented with secondary deposits in the lymph nodes, whereas in males primary growths of the cord metastasize only in the later stages. About three-quarters of the patients were treated by combined surgery and irradiation, the rest receiving radiation only; only a few had the benefit of modern technique. The results were relatively good; 15 patients, most of them with advanced disease, have died, mostly within 6 to 12 months of treatment, but the remaining 11 have survived more than 5 years. This is considered satisfactory in view of the high proportion of cases of secondary involvement and extensive primary growth.

J. Walter

Urogenital System

384. **Concentration of the Urine in Normal Subjects and Those with Renal Failure.** [In English]
M. H. ROSCOE. *Acta medica Scandinavica* [*Acta med. scand.*] **164**, 395–406, 1959. 3 figs., 11 refs.

When the volume of the urine is reduced by dehydration or by small doses of vasopressin there is an initial increase in osmolarity, but below a certain critical rate of flow this increase ceases or is even reversed. This suggests that at the critical rate of flow the urine represents fluid from the proximal tubules, and that this is modified by distal reabsorption or secretion of water at lower and higher rates of flow respectively. However, it has been shown that the urine at the critical rate of flow is more concentrated than plasma, whereas fluid from the proximal tubules is iso-osmotic with plasma, so water must have been reabsorbed in the collecting ducts.

The present author, working at the University of Manchester, has studied this " free water reabsorption " in 5 normotensive and in 22 hypertensive subjects, 16 of whom had renal failure and low glomerular filtration rates. The free water reabsorption was found to vary with the volume of the fluid carrying the solute load in a solution iso-osmotic with plasma. In the hypertensive subjects with normal filtration rates the solute output and free water reabsorption were lower than in the normotensive subjects, but the proportion of the solute water reabsorbed was no different. However, the volume reabsorbed decreased in those subjects with filtration rates of less than 80 ml. per minute, irrespective of the load. These results (with others reported in detail in the paper) suggest that concentration of the urine is brought about by a constant hyperosmolarity in the renal papillae, which produces reabsorption of a constant proportion of the fluid entering the collecting ducts. The failure of this " free water reabsorption " in renal insufficiency may be due to lowered osmolarity in the renal papillae.

[Those interested in renal physiology will wish to consult the original paper.] *T. B. Begg*

385. **The Kidney in Waldenström's Macroglobulinaemia.** (Le rein de la macroglobulinémie de Waldenström)
P. MICHON, G. RAUBER, A. LARCAN, and F. STREIFF. *Presse médicale* [*Presse méd.*] **67**, 1267–1270, June 24, 1959. 8 figs., 24 refs.

On the basis of a survey of the published reports of some 200 cases of Waldenström's macroglobulinaemia and of 7 cases seen personally at the Hôpital Central, Nancy, the authors stress the frequency of manifestations of renal abnormalities in this condition. These include azotaemia, albuminuria, Bence Jones proteinuria (revealed by immuno-electrophoresis and by precipitation and resolution on heating), and hyaline casts. Urinary-tract infections are common. Histologically, the kidney shows interstitial infiltration with lymphocytes and plasma cells, and there is often thickening of the glomerular basement membrane. The tubules may contain casts and the epithelium may be flattened, while foreign-body giant cells have been noted. Waldenström and Hehlinger have reported the occurrence of renal amyloidosis in association with macroglobulinaemia.

The authors relate these lesions to those found in myelomatosis and cryoglobulinaemia, propose a new aetiological classification—dysglobinaemic nephropathy—for such lesions, and discuss their pathogenesis.

Victor M. Rosenoer

386. **Blood Volume in Patients with Acute Glomerulonephritis as Determined by Radioactive Chromium Tagged Red Cells**
S. EISENBERG. *American Journal of Medicine* [*Amer. J. Med.*] **27**, 241–245, Aug., 1959. 22 refs.

At the Veterans Administration Hospital, Dallas, Texas, the blood volume in 10 patients with acute glomerulonephritis was determined during the acute phase of the disease and again after apparent recovery. Of the 10 patients, 9 recovered completely, but in one significant nitrogen retention developed associated with persistent microscopic haematuria. The blood volume was determined by the radioactive labelled erythrocyte technique. In 9 patients the total blood volume was significantly increased (25%) during the oedematous phase of the disease. The erythrocyte mass was little changed, but there was a 34% increase in plasma volume when the patient was oedematous. In one patient in whom blood volume was not studied until after the onset of diuresis the haematocrit value before and after diuresis indicated similar changes in the plasma volume. In 2 patients both labelled erythrocyte and dye-dilution techniques were used to determine plasma volume. By either technique the plasma volume was found to be expanded, but the values obtained with the dye technique were somewhat higher than those obtained with labelled erythrocytes. It is suggested that the " anaemia of acute glomerulonephritis " may be a dilution phenomenon, and that some of the " congestive " features attributed to cardiac failure may in fact be due to hypervolaemia. *C. Bruce Perry*

387. **Type Specific Antibodies in Acute Glomerulonephritis.** [In English]
I. CULLHED, I. JUHLIN, I. WERNER, and G. LAURELL. *Acta medica Scandinavica* [*Acta med. scand.*] **165**, 17–24, 1959. 33 refs.

388. **The Effect of ACTH and the Steroid Drugs on the Nephrotic Syndrome**
L. EALES. *South African Journal of Laboratory and Clinical Medicine* [*S. Afr. J. Lab. clin. Med.*] **5**, 125–155, Sept., 1959. 8 figs., 39 refs.

Endocrinology

389. **Cushing's Syndrome: Clinical Differential Diagnosis and Complications**

L. M. HURXTHAL and J. B. O'SULLIVAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **51**, 1–16, July, 1959. 26 refs.

As Cushing's syndrome is a potentially fatal condition, and since recent advances in the management of the disease have considerably improved the prognosis, its early recognition is of great importance. The present authors have therefore re-examined the early symptoms and problems of diagnosis in a series of 34 cases seen at the Lahey Clinic, Boston. There were 27 female patients and 7 males. In 27 cases the diagnosis was confirmed surgically and in 7 it was based on characteristic clinical signs and laboratory findings. The clinical onset was rapid in 24 cases, 5 being of such clear-cut remittent character that the onset might be termed "episodic"; in the remaining 10 cases it was gradual. There were no aetiological differences between these two groups, both containing examples of adrenocortical hyperplasia, adrenocortical adenoma, and aberrant adrenal tissue in the pancreas. In those with a rapid onset the common initial symptoms were oedema of the face and legs, rapid gain of weight, amenorrhoea (which might or might not be associated with either of the preceding features), renal colic, physical weakness, and mental disturbances. The differential diagnoses that had been considered in these cases were hypothyroidism (7), hyperthyroidism (3), nephritis or nephrosis, cardiac oedema, allergy, simple obesity, idiopathic renal calculi, collagen disease, and psychosis. Facial oedema was present in 14 cases and, it is suggested, is probably attributable to a combination of factors, including the tendency to hypoproteinaemia, hypernatraemia, and vascular fragility. In the cases of gradual onset a more gradual weight gain, oligomenorrhoea and hirsutism, diabetes mellitus, hypertension, mental disturbances, and osteoporosis were common presenting features which made the differential diagnosis from the other causes of such manifestations difficult. Among the helpful pointers to the diagnosis in such cases are the combined appearance of signs, high haemoglobin level, leucocytosis with relative lymphopenia and eosinopenia, severe fatigue and weakness, nervous complaints, and development of "moon face".

The authors differentiate those features which should be regarded as signs—for example, hypertension (88%) and osteoporosis (53%)—from those which are complications, such as pathological fractures (32%) and renal calculi (30%). They discuss the cardiovascular complications which may result from the hypertension and the susceptibility of patients with Cushing's syndrome to infection. Three of their patients developed duodenal ulceration, and 3 others peripheral neuritis of the Guillain–Barré type. They suggest that the latter may be a direct result of the disease process. *B. M. Ansell*

PITUITARY GLAND

390. **Sulfation Factor Activity of Sera from Patients with Pituitary Disorders**

W. H. DAUGHADAY, W. D. SALMON, and F. ALEXANDER. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **19**, 743–758, July, 1959. 9 figs., 15 refs.

Previous studies have shown that the rate of incorporation of radioactive sulphur (^{35}S) into the tibial epiphysis of young rats is greatly diminished after hypophysectomy, but can be restored to normal by treating the animals with small amounts of growth hormone. This procedure is valid for the assay of purified growth hormone, but is unreliable when applied to impure preparations or to human serum. For the studies here reported from Washington University School of Medicine, St. Louis, an *in-vitro* system was therefore devised whereby isolated pieces of costal cartilage from hypophysectomized rats are incubated in a medium containing glucose, amino-acids, buffer, the serum to be tested, and sulphate containing ^{35}S. After incubation the pieces of cartilage are washed and dried, hydrolysed, and the amount of radioactivity measured. From a comparison with the level of radioactivity in the incubation medium the amount of ^{35}S incorporated into the cartilage can be calculated. The factor responsible for promoting the incorporation of sulphate is called the sulphation factor and is measured by comparison with the activity of a reference pool of serum from a healthy young man. The relations between the sulphation factor and growth hormone are obscure, but the two are certainly not identical. Thus growth hormone itself is inactive in the *in-vitro* system and sulphation activity is not increased in the serum until several hours after the administration of growth hormone. That the two are related is shown by the virtual disappearance of sulphation factor from the serum of hypophysectomized rats and its reappearance after the administration of growth hormone.

In the present studies measurement of the sulphation factor in the sera of 29 persons between the ages of 7 and 73 revealed no difference in this activity at different ages; nor was there any significant diurnal variation in activity at different times of the day in 3 individuals so examined. Almost all the sera from these normal individuals showed an activity ranging between 0·4 and 1·5 times the activity of the reference standard. The activity in sera from 3 cases of pituitary dwarfism and from 5 cases of Sheehan's syndrome was well below the normal range, varying from 0·08 to 0·27. The relative activity was even lower (0·06 to 0·26) in sera from 9 patients who had undergone hypophysectomy. The residual activity still present in these patients, like that in hypophysectomized rats, is attributed to unidentified dialysable components in the serum. In 2 cases of craniopharyngioma and 6 of chromophobe adenoma the activity tended to be subnormal after operation, but in 2

further cases of chromophobe adenoma activity was normal, despite reduced thyroid and gonadal function, this perhaps indicating that there was some production of growth hormone by the tumour.

In contrast, sulphation-factor activity was high (3·7 to 8·2) in 7 of 16 acromegalics; this was usually found in the early active phase of the disease, levels nearer to normal being obtained later. In 2 of these cases successive assays made during the course of treatment showed high initial values, followed by a fall to nearer normal values after betatron therapy or x-irradiation of the pituitary gland. Significant increases in activity were found in one hypophysectomized woman given human growth hormone and in 2 patients with hypopituitarism who received monkey growth hormone. Daily assays in 3 cases of pituitary dwarfism given daily injections of human growth hormone also showed doubling or trebling of the originally low values, but this increase usually only began on the second day of treatment.

Peter C. Williams

THYROID GLAND

391. **The Free Achilles Reflex during Treatment of Hyperthyroidism**

J. D. Lawson and A. S. Weissbein. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **238**, 39–44, July, 1959. 4 figs., 8 refs.

In this paper from the Brooke Army Hospital, Fort Sam Houston, Texas, the authors describe the changes in muscle contraction time occurring during treatment of hyperthyroidism in a series of 44 patients. A new instrument, the kinemometer, an electromagnetic device connected to a standard electrocardiograph, was used to measure the contraction time of the gastrocnemius muscle following stimulation of the tendo achillis.

Before treatment all the patients had a muscle contraction time of between 110 and 160 milliseconds; with treatment this contraction time gradually increased to reach its maximum of 180 to 210 milliseconds after a period of 4 to 7 months. Of the 44 patients, 18 were operated on after an initial period of treatment with propylthiouracil, 22 received radioactive iodine, and 4 received propylthiouracil only. There was no appreciable difference between these three treatment groups in the rate of change of the muscle contraction time, an interval of about 6 weeks elapsing after the start of treatment before any change occurred. There was good correlation between clinical improvement and the prolongation of the muscle contraction time.

H. F. Reichenfeld

392. **Methimazole and Carbimazole in Hyperthyroidism: a Comparison by a Double Blind Technique**

T. H. McGavack. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **238**, 1–12, July, 1959. 23 refs.

A comparative study of the efficacy and toxicity of methimazole and carbimazole, both imidazole derivatives, in 123 patients with thyrotoxicosis is reported from the New York Medical College, a double-blind technique being used. The ages of the patients (26 male and 97 female) ranged from 16 to 83 years (average 43·8 years). Of the 68 patients who initially received methimazole, 54 later received carbimazole; of 55 who started treatment with carbimazole, 26 were later given methimazole. Except when side-effects appeared early each patient continued to receive the initial drug for not less than 10 weeks. No change in the dosage became necessary at the change-over; further, the comparable efficacy of the two drugs was demonstrated by the fact that the initial controlling dose for each of the two compounds ranged from 30 to 60 mg. daily.

With either drug initial improvement was noticed on the average after one week's treatment (range 3 to 14 days) and the thyrotoxic state was controlled after an average of 4½ weeks' treatment. Side-effects, which included pruritus, rash, oedema, or a combination of these, occurred in 6 patients receiving methimazole and in 5 given carbimazole. In addition urticarial febrile reactions developed in 2 patients receiving methimazole. Some of these side-effects disappeared spontaneously, while others became less when the dosage of the drug was reduced or a change made to the other drug. However, some patients could not tolerate either of the two compounds. Bone-marrow reactions were not observed, but a transient polymorphonuclear leucopenia was seen occasionally.

H. F. Reichenfeld

393. **Evaluation of Radioactive Iodine (I^{131}) as a Treatment for Hyperthyroidism**

C. E. Cassidy and E. B. Astwood. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 53–58, July 9, 1959. 26 refs.

An analysis is presented of the results in 200 patients treated with radioactive iodine (^{131}I) for hyperthyroidism at the New England Center Hospital (Tufts University School of Medicine), Boston. The indications for this form of treatment varied, but recently they have included associated cardiovascular disease, postoperative recurrence of the initial disorder, recurrence after two courses of antithyroid drugs, very large goitres, and long-standing or severe hyperthyroidism. No children were treated, but otherwise no arbitrary age limit was applied. The initial dose of ^{131}I was calculated by the formula of Werner *et al.* (*Radiology*, 1948, **51**, 564; *Abstr. Wld Med.*, 1949, **6**, 84) and usually amounted to 10,000 r.e.p. When the effective half-life was not actually determined it was assumed to be 5 days. However, the dose given was often selected empirically for a second dose (and occasionally also for a first dose). About half the patients (49%), that is, those with severe hyperthyroidism, received an antithyroid drug for an average of 10·4 weeks, beginning 24 to 48 hours after administration of the therapeutic dose of ^{131}I.

Of the 200 patients, 171 (85·5%) ultimately became euthyroid, while the remaining 14·5% developed permanent hypothyroidism. In 131 cases (65·5%) only one treatment dose was given and of these, 22 (17%) became permanently myxoedematous; in 47 cases (23·5%) two doses were given, and in the remaining 11% three to

seven doses. No complication of any kind was seen except for temporary or permanent hypothyroidism. The late development of hypothyroidism was observed in several patients 2 to 5 years after treatment. A follow-up of 90 of the 101 patients treated before 1954 and previously reported by Anderson (*Metabolism*, 1954, **3**, 297; *Abstr. Wld Med.*, 1955, **17**, 47) showed that 23 (26%) had developed myxoedema. Many factors were analysed in regard to their effect on the response to treatment, but no significant correlation could be established between such response and dose of ^{131}I administered, thyroid mass, effective half-life, age, sex, previous treatment, or nodularity of the gland. Myxoedema occurred significantly less often in patients treated with antithyroid drugs after injection of ^{131}I than in those treated with ^{131}I alone. More patients with recurrent hyperthyroidism needed more than one treatment dose than in the group previously reported, but the incidence of myxoedema in the two groups was not significantly different.

K. E. Halnan

394. **Peripheral Neuropathy in Myxedema**

L. E. Crevasse and R. B. Logue. *Annals of Internal Medicine* [*Ann. intern. Med.*] **50**, 1433–1437, June, 1959. 11 refs.

To determine the incidence of peripheral neuropathy in myxoedema the authors, at Emory University School of Medicine, Atlanta, Georgia, reviewed the records of 65 patients with idiopathic myxoedema. It was found that 31 of the patients had had burning pains in the extremities and/or troublesome paraesthesiae which were considered to be related to the myxoedema. Detailed case records of 3 patients showed that pain in both legs, inability to walk, cramp, and absence of sensation in the limbs might all be early symptoms of myxoedema. The authors note that these symptoms may be confused with those seen in pernicious anaemia, myasthenia gravis, cord tumour, or disseminated sclerosis, particularly if classic manifestations of myxoedema are not obvious. Symptoms of peripheral neuropathy clear up satisfactorily with adequate thyroid treatment. *Charles Rolland*

395. **Observations on the Effect of Potassium Perchlorate on Thyroid Function**

R. C. Dickson, W. I. Morse, and J. E. Stapleton. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **81**, 12–15, July 1, 1959. 5 figs., 6 refs.

The antithyroid effect of potassium perchlorate has been studied by the authors at Victoria General Hospital and Dalhousie University, Halifax, Nova Scotia. It was shown by Vanderlaan and Vanderlaan (*Endocrinology*, 1947, **40**, 403; *Abstr. Wld Med.*, 1948, **4**, 296) that in rats treated with thiouracil potassium thiocyanate prevented the accumulation of iodine in the thyroid gland and also caused the discharge of such iodine as was present in the gland in the form of iodide. Wyngaarden *et al.* (*Endocrinology*, 1952, **50**, 537; *Abstr. Wld Med.*, 1952, **12**, 542) subsequently showed that potassium perchlorate behaved in a similar way, but was more potent. Both blocking and flushing effects of potassium chlorate have been further studied in man by the present authors.

When 400 mg. of potassium chlorate was given one hour after a tracer dose of radioactive iodine (^{131}I) to a euthyroid and a hyperthyroid patient no decrease in the ^{131}I content of the gland was noted during the following hour. In contrast, when ^{131}I followed by the same dose of potassium perchlorate was given to a normal volunteer previously treated with methimazole there was marked flushing of iodine from the thyroid gland which was comparable with that seen in a patient with Hashimoto's thyroiditis. A dose of 20 mg. of potassium chlorate given together with ^{131}I failed to produce any significant block in the thyroid uptake of ^{131}I in a normal subject, but a dose of 200 mg. produced a striking block which was effective for at least 24 hours. In a hyperthyroid subject, however, although the 24-hour uptake of ^{131}I was reduced from 95% to 32%, the full blocking effect lasted only 4 hours after administration of the drug.

Control of hyperthyroidism with potassium perchlorate was attempted in 24 patients, including 2 adolescents. In 4 cases it was abandoned owing to failure to respond (one case) or toxic side-effects (3 cases). In 4 others a dose of 250 mg. twice daily was given and found unsatisfactory. Ten patients were treated with 100 mg. 5 times daily and 6 with 200 mg. 5 times daily; the latter dosage gave the most satisfactory clinical response, and this was confirmed by comparing the regression times of the mean serum protein-bound iodine (P.B.I.) levels in the two groups. The average time taken to reduce the P.B.I. level to 6 μg. per 100 ml. was 13 weeks with 100 mg. and 8 weeks with 200 mg. of the drug 5 times daily compared with the 6 weeks required to render patients euthyroid with methimazole and iodine.

Drug rashes and occasional failure to respond were the chief disadvantages of the drug, and it was also noted that in some cases there was an exacerbation of symptoms of hyperthyroidism in the first 2 weeks of treatment. In a further trial 6 euthyroid patients with angina pectoris were treated with 100 mg. of potassium perchlorate 5 times daily for periods up to 7 months, none being rendered hypothyroid by this treatment.

The authors conclude that potassium perchlorate is effective as an antithyroid drug in most cases of hyperthyroidism. A particular advantage was the absence of signs of hypothyroidism even with long-term therapy, and this makes it a suitable preparation for the treatment of adolescents and also of euthyroid patients suffering from angina pectoris. *John Lister*

396. **Rapidly Acting Thyroid Hormones and Their Cardiac Action**

K. Ibbertson, R. Fraser, and D. Alldis. *British Medical Journal* [*Brit. med. J.*] **2**, 52–58, July 18, 1959. 10 figs., 38 refs.

This paper from the Postgraduate Medical School of London reports studies of the action of two synthetic thyroid hormones, triiodothyronine and its acetic acid derivative (" triac "), on patients with myxoedema.

Six myxoedematous patients without evidence of coronary arterial disease who were under 40, had not had myxoedema long, or had been treated for it were given large single doses of one or other hormone or a placebo

on a total of 18 occasions. On each occasion the patient was given repeated doses of sodium amylobarbitone to produce sleep for 26 hours from 7 a.m. The basal metabolic rate (B.M.R.) was measured at the time that the test drug was given (9 a.m.) and again 2, 4, 6, 8, 10, and 24 hours later. The initial reading was expressed as a percentage of the expected normal and each later result was then expressed as a percentage of the initial one. When the placebo was given the B.M.R. fell slightly through the day. After the administration of triac (6 to 18 mg.) the B.M.R. rose in all of 10 trials; the rise was apparent by the 4th hour after the dose and reached a peak of about 50% above the initial value between the 6th and 24th hours. A similar rise occurred after the administration of 0·5 mg. of triiodothyronine to 4 of the patients. Each time the B.M.R. was measured an electrocardiogram (ECG) was recorded. The voltage of the R wave of the ECG was found to be the most sensitive index of thyroid hormone activity. It rose after the administration of triac in all cases, usually by 60 to 100% and often by the 4th hour; after triiodothyronine the rise occurred later and was less marked. The plasma cholesterol level was estimated several times in the first 24 hours after giving the test drug and then daily for about a week; the level fell in all cases, usually within 24 hours and sooner after triac than after triiodothyronine. An increased urinary output of creatine was observed in 3 out of 4 cases in the first 24 hours after triac, but not after triiodothyronine. This increase lasted for 3 days only, whereas the other effects of both hormones continued for 6 to 10 days.

Two of these patients and 4 others were then given triac daily in various doses. Three received 0·5 to 1 mg. daily at first, and in 2 of them the plasma cholesterol level fell before any other effect was noted—as also occurred in 2 other patients who were given a small daily dose of triiodothyronine. Patients who were given 5 mg. daily of triac showed a gradual return of all parameters to the normal level in 7 to 10 days. Triac was also given in small doses to 14 other patients with myxoedema, starting with 0·25 to 0·5 mg. and increasing gradually, when possible, to a maintenance dose of 4 to 6 mg. daily. Three with a history of angina developed symptoms of cardiac ischaemia even on the smaller dosage. *G. C. R. Morris*

397. **Cytotoxic Effects of Hashimoto Serum on Human Thyroid Cells in Tissue Culture (Preliminary Communication)**

R. J. V. Pulvertaft, D. Doniach, I. M. Roitt, and R. V. Hudson. *Lancet* [*Lancet*] **2**, 214–216, Aug. 29, 1959. 4 figs., 9 refs.

In investigations reported from the Westminster and Middlesex Hospital Medical Schools, London, monolayers of thyroid gland cells were prepared from surgically excised human tissue by trypsin dispersal of the cells. The preparations were cultured in small chambers attached to microscope slides. The culture medium consisted of 50% test or control serum mixed with 50% diluent, which was either Hanks fluid with 0·1% "difco" yeast extract or the synthetic medium 199 of Morgan *et al.* (*Proc. Soc. exp. Biol.* (*N.Y.*), 1950, 73, 1). Thyroid cells grown in a medium made with normal serum survived unchanged for a period of 18 days. When the medium was made up with serum from patients with Hashimoto's disease there were few or no surviving thyroid cells after 18 hours, though lymphocytes, monocytes, and polymorphonuclear granulocytes retained a normal appearance and motility. When normal serum was replaced by Hashimoto serum after 18 to 24 hours cytotoxic changes commenced within 30 seconds. Hashimoto sera destroyed cells grown from the patient's own thyroid gland as well as those from thyrotoxic and non-toxic nodular glands. The cytotoxic effect of Hashimoto serum was destroyed by heating it to 56° C. and activity was not restored by the addition of fresh guinea-pig complement. Thyroid cells grown in normal serum for 36 hours or more were not affected by Hashimoto serum. The significance of these results is discussed. *P. A. Nasmyth*

398. **Endemic Goiter and Nutrition. I. A Study of Some Aspects of Their Relationship in a Brazilian Amazon Community**

F. W. Lowenstein. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **7**, 331–338, May–June, 1959. 1 fig., 14 refs.

In 1956 a dietary and clinical survey was carried out among 84 families, representing 413 individuals, in Belterra, Brazil, a 25-year-old rubber plantation community of low socio-economic and educational levels, the object being to determine the relationship between endemic goitre and nutrition. The daily intake of calcium, vitamin A, and the B group of vitamins was found to be grossly inadequate when compared with the daily allowances recommended by the National Research Council of the U.S., the daily consumption of calcium being 11 to 19% of the recommended standard, of vitamin A 5 to 14%, and of the B group of vitamins 46 to 80%. Analysis of the water supply revealed complete absence of iodine and fluorine. The percentage incidence of goitre was 30 to 35 in the age group 0 to 5 years, 66 to 77 in the age group 6 to 10, 32 to 55 in individuals aged 11 to 20 years, and 15 to 40 in those over 21. In children aged 6 to 18 years the incidence of caries was 98% for girls and 100% for boys. There were 2 cases of moderately severe kwashiorkor in children aged 1 to 2 years, but in older children and adults no evidence of protein deficiency was found. Conjunctival spots, increased calf tenderness, and circumcorneal congestion were present in a few cases; the incidence of other signs of nutritional deficiency was low. *H. E. Magee*

399. **Endemic Goiter and Nutrition. II. A Follow-up Study of 75 Families in a Brazilian Amazon Community**

F. W. Lowenstein. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **7**, 339–348, May–June, 1959. 2 figs., 12 refs.

Of the 84 families studied in 1956 [see Abstract 398] 75 were followed up one year later (381 of the original 413 individuals). During the year wages and purchasing power had much improved. The daily consumption of

all nutrients except calcium and vitamin A compared very favourably with the daily consumption recommended by the National Research Council of the U.S., and there was less evidence than in the earlier survey of deficiency of the B group of vitamins. While dental caries and goitre were still the chief problems, there was evidence of some improvement as regards goitre: in 40 (28·8%) of the 139 cases of goitre recorded in 1956 there was complete regression and in 36 cases there was regression from severe goitre to a milder form. However, there was a slight increase of 6·3% in the total incidence of goitre. *H. E. Magee*

400. **Angiographic Aspects of Disease of the Thyroid: an Evaluation of Subclavian Retrograde Arteriographic Procedures as a Means of Clinical Study**
A. Bobbio, E. Bezzi, E. Zanella, and L. Rossi. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] 32, 79–97, July, 1959. 17 figs., 3 refs.

This paper from the University of Parma gives a well illustrated account of angiographic studies of thyroid swellings made by the introduction of 20 ml. of contrast medium (70% " renografin ") into the subclavian artery, a piece of rubber tubing being used as an arterial tourniquet at the root of the arm. The patient lies with the shoulder depressed and the needle is introduced above the mid-point of the clavicle.

Serial radiographs show an arterial phase at 1 to 4 seconds, an arterio-capillary phase at 5 seconds, a capillary phase at 7 to 8 seconds, and a venous phase at 9 to 11 seconds. This last is rarely visualized in the normal gland, but is evident when the circulation through the thyroid is retarded or accelerated. General anaesthesia is preferred and the technique employed has been to obtain right and left arteriograms separately, allowing half an hour to elapse between the two.

Illustrative examples are given of angiographic studies of various diseases of the thyroid, including a case of carcinoma. The authors anticipate that information obtained by this technique will be particularly useful in posterior mediastinal goitre, which has not yet been studied.

[Although this new method is pictorially attractive, it seems as yet to offer less diagnostic aid than isotope studies or radio-autography. In differentiating Hashimoto's disease it cannot, of course, compare with antibody tests.] *Guy Blackburn*

401. **Relationship between Thyroid Function and the Basophil Leucocytes.** (Rapporti tra funzionalità tiroidea e leucociti basofili)
F. Cavazzuti, G. Tedeschi, and G. Angeli. *Minerva medica* [*Minerva med. (Torino)*] 50, 2352–2358, July 21, 1959. 4 figs.

After a brief review of the literature concerning the haematological activity of the thyroid hormone the authors report investigations carried out at the Institute of General Clinical Medicine and Medical Therapeutics of the University of Modena into the relation between thyroid function and the basophil leucocyte count in the peripheral blood. Basophil counts were performed on 60 euthyroid, 41 hyperthyroid, and 4 hypothyroid subjects under 60 years of age and on 30 euthyroid and 3 hypothyroid subjects over 60. The technique used was that developed by the authors and described elsewhere. A statistical evaluation of the results was carried out whenever possible.

A significant increase in the basophil count by an average of 62% over the control value was found in the hypothyroid patients, and a diminution, also by an average of 62%, in the hyperthyroid patients under 60. The abnormality of the basophil count showed an inverse relation to the basal metabolic rate and especially to the serum protein-bound iodine value. These observations were confirmed by further studies during treatment and by experimental studies in man and animals after the administration of thyroid stimulating hormone, thyroxine, and 1-methyl-2-mercaptoimidazol (in the form of " bromazol "). The method is regarded as sufficiently simple, reliable, and practical to be included in the standard practice of the clinical laboratory, and as providing a useful additional diagnostic test in cases of thyroid dysfunction.

[It is regrettable that the technique, which is claimed to be so simple, is not described in greater detail, especially since references to the authors' previous work and that of the numerous others cited are omitted from the original paper, the bibliography being available only with the authors' reprints. This short-sighted editorial policy greatly detracts from the value of the paper and of the journal in which it is published.] *V. C. Medvei*

DIABETES MELLITUS

402. **Interrelations of Tolbutamide and Glucagon**
C. K. Gorman and J. A. Weaver. *Lancet* [*Lancet*] 2, 21–22, July 11, 1959. 8 refs.

The effect of tolbutamide on the response to glucagon has been studied in 12 diabetic patients. The capacity of glucagon to raise the blood-glucose was unaffected by the preliminary administration of tolbutamide.—[Authors' summary.]

403. **Effects of Insulin and Tolbutamide on Production and Utilization of Blood Sugar**
G. A. Reichard Jr., A. G. Jacobs, B. Friedmann, P. R. Kimbel, N. J. Hochella, and S. Weinhouse. *Metabolism: Clinical and Experimental* [*Metabolism*] 8, 486–493, July, 1959. 6 figs., 24 refs.

In experiments carried out at the Albert Einstein Medical Center and the Home for the Jewish Aged, Philadelphia, the rate of disappearance of radioactive carbon (^{14}C) from the blood following the injection of a tracer dose of glucose uniformly labelled with ^{14}C was studied and the effect on this rate of the administration of insulin and of tolbutamide determined. In the normal fasting dog and man the rate of disappearance of ^{14}C was found to follow an exponential curve, indicating steady uptake of the labelled glucose and its replacement from unlabelled sources. Injection of insulin resulted in a plateau in the graph of the ^{14}C level during the period

of precipitate fall in blood sugar level, the exponential fall being renewed when the blood sugar level began to rise again. This is interpreted as evidence that insulin primarily blocks the output of glucose from the liver. When glucagon or glucose was injected in sufficient quantity to induce hyperglycaemia there was a precipitate fall in the ^{14}C level, indicating the dilution of labelled with unlabelled glucose, followed by a plateau in the curve of specific activity when the blood sugar level reached its maximum. This is interpreted by the authors as indicating the suppression of hepatic glucose release by hyperglycaemia.

The results of similar experiments with tolbutamide and with infusions instead of single injections of insulin supported the concept that the hypoglycaemic action of tolbutamide is an insulinogenic one mediated through the suppression of hepatic glucose output, which represents the primary site of action of insulin.

F. W. Chattaway

404. **The Effect of Insulin on Hepatic Glucose Metabolism in the Unanesthetized Dog**

W. C. SHOEMAKER, R. MAHLER, and J. ASHMORE. *Metabolism: Clinical and Experimental* [*Metabolism*] **8**, 494–511, July, 1959. 12 figs., 32 refs.

Experiments are reported from Harvard Medical School, Boston, the University of Indiana Medical School, Indianapolis, and the Michael Reese Hospital, Chicago, in which glucose concentrations were measured in blood from the hepatic artery and vein and the portal vein in unanaesthetized dogs and information thus gained of the glucose gradients in the entire splanchnic area, in the liver, and in the non-hepatic splanchnic area. Administration of insulin resulted in a decreased total splanchnic glucose output, but this was shown to be due to uptake of glucose by the non-hepatic splanchnic area, there being no immediate effect upon glucose output by the liver. Experiments with glucose labelled with radioactive carbon (^{14}C) supported this view; the plateau in the curve of specific activity of the plasma following insulin administration was most marked in portal venous blood, the liver gradient of ^{14}C being unaltered by insulin injection.

Thus the changes in blood sugar level following insulin which are usually ascribed to an effect on the liver may be explained by an uptake of glucose by mucosal cells and its subsequent release in response to insulin-induced hypoglycaemia.

F. W. Chattaway

405. **Variability in Absorption of Insulin–I^{131} in Normal and Diabetic Subjects after Subcutaneous and Intramuscular Injection**

E. W. MOORE, M. L. MITCHELL, and T. C. CHALMERS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **38**, 1222–1227, July, 1959. 4 figs., 15 refs.

The rate of absorption of insulin labelled with radioactive iodine (^{131}I) after subcutaneous and intramuscular injection was studied in 22 diabetic and 11 normal subjects at the Lemuel Shattuck Hospital and the Harvard and Tufts University Medical Schools, Boston. The ages of the diabetic patients ranged from 25 to 70 years and their daily insulin requirements from 15 to 70 units. Doses of 0·05 to 0·4 unit of insulin containing 15 to 30 μc. of ^{131}I-insulin were injected into the deltoid area 1½ to 2 hours after the daily dose of normal insulin, and radioactivity at the injection site was assessed with a collimated scintillation counter at hourly intervals for 8 hours and again at the end of 24 hours.

The curve of absorption of insulin injected subcutaneously was exponential in both groups, and with equal doses of insulin was more rapid when given in a larger volume, although not significantly so in the diabetics. In individual diabetics there was some variation in the rate of absorption from the two arms and also from the same arm at different times. No significant difference was found between rates of absorption in normal and diabetic subjects with comparable injection volumes. Comparison of the rate of absorption of insulin given subcutaneously and intramuscularly simultaneously to 7 normal subjects showed no significant difference, but in 5 diabetic patients intramuscular injection resulted in significantly faster absorption than subcutaneous injection. After 24 hours residual radioactivity at the site of intramuscular injection was significantly greater than after subcutaneous injection in both normal and diabetic subjects, and was also significantly greater in the diabetics than in the normal subjects. Two diabetic patients showed a very delayed absorption of subcutaneously injected insulin from one arm, while absorption from the other arm was normal, this being possibly attributable to relative avascularity of one arm.

The authors conclude that considerable variation can occur in the rate of absorption of insulin from the tissues, and suggest that tissue binding of insulin may occur in muscle following intramuscular injection in both normal and diabetic subjects.

Gerald Sandler

406. **Further Studies on the Mechanism of Action of Insulin**

R. C. DE BODO, R. STEELE, N. ALTSZULER, A. DUNN, D. T. ARMSTRONG, and J. S. BISHOP. *Metabolism: Clinical and Experimental* [*Metabolism*] **8**, 520–530, July, 1959. 6 figs., 14 refs.

At the New York University College of Medicine and Brookhaven National Laboratory, Upton, New York, the effects of insulin on the blood glucose level have been studied in unanaesthetized dogs by giving glucose labelled with radioactive carbon (^{14}C) by constant infusion at such a rate as to balance the output of endogenous ^{12}C-glucose by the liver under normal resting conditions. In such circumstances if the fall in plasma glucose concentration following the injection of insulin is due to a decrease in glucose output by the liver the specific activity of the plasma glucose should rise. If, however, the fall is due to increased tissue uptake of glucose then the balance between infused ^{14}C-glucose and endogenous ^{12}C-glucose will be unchanged and the specific activity should be unaltered.

Experiments with single injections and infusions of insulin and with injections of glucose to increase endogenous insulin production all indicated that the effect of insulin was to increase the tissue uptake of glucose.

It was also noted that during the prolonged infusion of insulin the output of glucose from the liver did not rise above the pre-insulin level until the infusion was stopped; thus while insulin did not reduce the glucose output of the liver, it did appear to prevent its increase.

F. W. Chattaway

407. **Clinical Trials with Phenethyldiguanide in Selected Patients**

R. E. TRANQUADA, C. R. KLEEMAN, and J. BROWN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **238**, 187–192, Aug., 1959. 8 refs.

In this paper from the University of California Medical Center and the Veterans Administration Hospital, Los Angeles, the results are reported of administration of phenethyldiguanide (" DBI ") in 30 patients with diabetes other than the stable adult form. The drug was given in a dosage of 25 to 50 mg. three times a day up to a maximum of 300 mg. daily. In 3 out of 12 patients with labile diabetes control of the disease was improved by a combination of DBI and less than half the previous dosage of insulin. Of 8 patients with onset of diabetes following pancreatectomy or with recurrent pancreatitis, 4 improved with a 50% reduction in insulin dosage. In 4 out of 10 patients whose daily insulin requirement was over 50 units the diabetes was better controlled by giving DBI and a reduced dosage of insulin. Side-effects developed in all but 3 of the patients and severely limited the usefulness of the drug. Severe anorexia occurred in 28 patients, nausea in 21, vomiting in 5, and malaise in 10. There was no evidence of liver, kidney, or bone-marrow dysfunction. In spite of the disadvantages it is considered that DBI may be helpful in the stabilization of labile or insulin-resistant diabetes and in the management of patients who are unresponsive to the sulphonylurea drugs or are unable to give themselves injections of insulin.

Kenneth Gurling

408. **A Critical Appraisal of Oral Hypoglycemic Agents.** [Review Article]

T. H. MCGAVACK. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 7, 681–697, Sept., 1959. 4 figs., bibliography.

409. **Reappraisal of the Hypoglycemic Action of Acetylsalicylate**

A. HECHT and M. G. GOLDNER. *Metabolism: Clinical and Experimental* [*Metabolism*] 8, 418–428, July, 1959. 20 refs.

The hypoglycaemic action of the acetylsalicylates was studied in 25 patients (aged 29 to 78 years) at King's County Hospital, Brooklyn, N.Y., including 12 diabetics of whom 9 required either insulin or oral hypoglycaemic agents. Acetylsalicylate was given in the form of standard aspirin tablets in a minimum daily dosage of 4·8 g. for 1 to 3 weeks. The fasting blood sugar was estimated twice a week. Oral and intravenous glucose tolerance tests and insulin tolerance tests were carried out before and after 1 or 2 weeks of salicylate administration. In 4 cases glucagon tolerance tests were performed during the period of treatment.

Salicylism developed in 2 patients and administration of the drug was stopped. In 12 of the 13 non-diabetic patients there was a fall in the fasting blood sugar level during salicylate treatment; the fall averaged 23 mg. per 100 ml. in 8 and was insignificant in 4. The oral glucose tolerance test revealed a lowering of all values in 7 out of the 10 non-diabetic patients.

In 9 of the 12 diabetic patients salicylate significantly lowered the blood sugar level. There was a marked lowering of the glucose tolerance curve, and the average fall in the fasting blood sugar level was 59 mg. per 100 ml. In responsive patients the dosage of insulin or tolbutamide could be reduced. There was a normal hyperglycaemic response to the glucagon tolerance test in all 4 cases in which this test was carried out.

In 2 patients in the series a hyperglycaemic response was obtained during treatment, but there were reasonable grounds for doubting whether this was due to the salicylate.

Charles Rolland

410. **Circulating Lipids in Diabetes Mellitus**

D. ADLERSBERG and L. EISLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1261–1265, July 11, 1959. 1 fig., 19 refs.

From Mount Sinai Hospital, New York, the authors report findings concerning the total lipid and fatty acid content of the serum as well as the serum cholesterol, phospholipid, and triglyceride levels in four groups of diabetic patients. Group 1 and Group 2 had no clinical evidence of cardiovascular or renal disease, findings which were confirmed radiologically and by means of electrocardiography. The groups differed in that Group 1 was well controlled, the blood sugar level being always below 150 mg. per 100 ml., whereas this was not so in Group 2. In Groups 3 and 4 there was evidence of coronary or peripheral arterial disease, but no evidence of renal disease, control in Group 3 being good (as in Group 1), and in Group 4 poor (as in Group 2).

There were no striking differences in the serum cholesterol and phospholipid levels between the four groups, but the fatty acid and triglyceride levels were decidedly higher in Group 2 than in Groups 1 and 3, and even more so in Group 4. Study was also made of the lipoprotein fractions by electrophoresis, but only in Group 4 did the pattern differ significantly from that in Group 1, there being a decrease in the α fraction and a corresponding increase in the O fraction. The numbers of patients in Groups 3 and 4 were small (11 and 14 respectively) compared with those in Groups 1 and 2 (44 and 25 respectively), and the period of medical observation varied in the whole series from 6 months to 12 years.

The authors emphasize that abnormalities in the circulating lipids in diabetes are related to two factors: (1) decompensation of deranged carbohydrate metabolism (lack of insulin); and (2) the presence of vascular complications. They conclude by suggesting that better control of carbohydrate metabolism, as indicated not only by the fasting blood sugar level but also by the blood lipid levels, might lead to a reduced incidence of pathological changes in the arteries in patients with diabetes.

R. E. Tunbridge

The Rheumatic Diseases

411. **Methylprednisolone (Medrol) in the Treatment of Systemic Lupus Erythematosus**
E. L. DUBOIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1537–1542, July 25, 1959. 10 refs.

The results in 40 cases of active systemic lupus erythematosus treated with methylprednisolone (" medrol ") over 16 months are reported from the University of Southern California, Los Angeles. In 15 of these cases antimalarial treatment was given concurrently.

The pattern of response was similar to that obtained with prednisone, triamcinolone, and other anti-inflammatory steroids, while the incidence of moon face, hirsutism, acne, and the formation of striae was about the same. The average daily dose of methylprednisolone for initial suppression was 29·2 mg. (range 8 to 96 mg.) and for maintenance 25·9 mg. per day. There was a high incidence of ecchymosis, which occurred in 27% of the patients compared with 14% with triamcinolone and 3% with prednisone. A new peptic ulcer appeared in only one case, which is described. Of the 18 patients who had received other steroids, only 2 had better control and felt better while taking methylprednisolone. Nevertheless this preparation is considered a relatively safe and potent anti-inflammatory agent for the treatment of systemic lupus erythematosus. *Oswald Savage*

412. **The Heart in Systemic Lupus Erythematosus.** [Review Article]
M. A. SHEARN. *American Heart Journal* [*Amer. Heart J.*] **58**, 452–466, Sept., 1959. Bibliography.

413. **Gout: Six-year Follow-up on Probenecid (Benemid) Therapy**
E. C. BARTELS and G. S. MATOSSIAN. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] **2**, 193–202, June, 1959. 4 figs. 10 refs.

Between 1951 and 1958 at the Lahey Clinic, Boston, probenecid was given in the treatment of 231 patients suffering from gout. The dosage of the drug was 0·5 to 1 g. daily, and with each 0·5 g. of probenecid 0·5 mg. of colchicine was also administered. The dosages were adjusted so that the serum uric acid level did not exceed 6 mg. per 100 ml. In one patient given 0·25 g. of probenecid daily for more than 3 years the serum uric acid level was maintained at approximately 4 mg. per 100 ml. Two months after treatment was discontinued the level rose sharply to 7·5 mg. per 100 ml. Comparatively high serum levels of uric acid were detected in patients with renal disease.

Patients were advised to abstain from alcohol and to restrict the amount of purines and fat in the diet. In order to avoid precipitating an acute attack of gout no attempt was made to bring about a reduction in weight until the disease was under good control. In the first year the average number of acute attacks declined from 3·6 to 1·3 and in the second year to less than one. Probenecid with colchicine appeared to be more effective than probenecid alone. Untoward reactions to probenecid, which were recorded in 21 cases, included gastrointestinal disturbances, rashes, headache, pruritus, and polyuria. In 2 of 3 cases in which urinary calculi were passed the calculi gave a positive reaction for urates. One patient experienced transient mental confusion. Radiological examination of the bones revealed arrest of the disease in 8 cases, including 4 in which recalcification was observed in punched-out areas. Diminution in the size of the tophi was demonstrated in 18 of 47 patients who received probenecid for at least 6 months. In 3 cases the disease failed to respond to treatment.

During the course of the investigation the authors studied the history and development of the disease. The age at onset was usually 35 to 39 years and the average weight of the patients was 37·3 lb. (17 kg.) higher than normal. It is concluded that tophaceous and non-tophaceous gout are clinical variants, and that the presence of renal disease is not essential for the development of tophi. *A. Garland*

ACUTE RHEUMATISM

414. **Relation of Isolated Recurrences of Sydenham's Chorea to Preceding Streptococcal Infections**
A. TARANTA. *New England Journal of Medicine* [*New Engl. J. Med.*] **260**, 1204–1210, June 11, 1959. 4 figs., 19 refs.

From New York University College of Medicine the author reports a study of 60 children with a history of chorea who were followed up by monthly examinations for 2 to 67 months (mean 40·7 months) at the Irvington House Rheumatic Fever Prophylaxis Clinic, Irvington-on-Hudson, with the aim of elucidating the relation between streptococcal infection, rheumatic fever, and chorea. At some time during the preceding 28 months all but 2 of the patients had had rheumatic fever (as defined by modified Duckett Jones criteria), the 2 exceptions having had only chorea. Each was given continuous prophylactic antistreptococcal treatment and at each visit a throat swab was taken, while the antistreptolysin-O and antihyaluronidase titres were determined at least every 2 months.

Of the 60 children, 41 developed no streptococcal infection during the follow-up period and there was no recurrence of chorea in these patients. The remaining 19 patients, however, developed such infection despite the prophylactic regimen and in 3 of these the chorea recurred, in one case twice. It is of interest to note that these four recurrences took place at intervals after the development of streptococcal infection (as judged by the

rise in antibody titre) of approximately 5, 70, 90, and 180 days respectively, with a mean of about 87 days. These periods are contrasted with the mean interval of 10 days between the rise in antibody titre and the onset of polyarthritis or carditis in the 29 children who, despite prophylaxis, suffered a recurrence of rheumatic fever. Detailed case reports are given of the 3 children in whom, it was observed, the recurrence of chorea was not preceded or accompanied by clinical evidence of rheumatic fever. Only one of the four recurrences was associated with a high erythrocyte sedimentation rate and a positive result in the test for C-reactive protein in the absence of clinical signs. These findings thus provide the first reported evidence that Sydenham's chorea can follow Group-A streptococcal infection at longer intervals than, and in the absence of, polyarthritis and carditis, and indeed in the absence of any sign of " rheumatic activity ".

E. G. L. Bywaters

415. **The Prophylaxis of Recurrent Rheumatic Fever.** (Prophylaxie des rechutes du rhumatisme articulaire aigu)

P. GIRAUD, R. BERNARD, A. HEURTEMATTE, M. SANSOT, P. LATIL, P. MAESTRAGGI, and C. MOINE. *Pédiatrie* [*Pédiatrie*] **14**, 337–341, 1959. 1 fig., 1 ref.

This paper records the results of penicillin prophylaxis in a group of children recovered from an attack of acute rheumatism in comparison with a similar group of children receiving no prophylaxis. The children were aged 3 to 16 years and the observations were continued for periods which varied from less than a year to 5 years. Among the treated children (210 in all), who received 600,000 units of benzathine penicillin intramuscularly every 10 to 15 days for a total period of 5,120 patient-months, there were 3 cases of relapse of acute rheumatism —a rate of 0·06 per 100 patient-months. Among the 190 children who received no prophylactic treatment after the initial attack and were followed up for a total of 8,282 patient-months there were 30 relapses—a rate of 4 per 100 patient-months. A smaller group of 50 children who received no specific prophylaxis, but were given " non-specific " prophylaxis in the shape of ultraviolet light, cod-liver oil, sea baths, or dietary supplements, was studied for 1,764 patient-months, 43 relapses being observed—a rate of 2·5 per 100 patient-months. The efficiency of penicillin prophylaxis is thus clear, but the general measures were apparently also of some value.

The length of time for which prophylaxis with penicillin should be maintained is discussed and it is shown that the majority of relapses occur within 4 years of the last attack. It is therefore suggested that prophylaxis should be maintained for a minimum of 4 years. It is further suggested that after regular prophylaxis has ceased " prophylaxis on demand " should be arranged by ensuring that when any rheumatic child develops a febrile illness a dose of penicillin adequate to eliminate haemolytic streptococci from the throat should be given without waiting to determine whether or not such organisms are present. A mixture of 600,000 units of benzathine penicillin, 300,000 units of procaine penicillin, and 300,000 units of benzylpenicillin is recommended.

C. Bruce Perry

CHRONIC RHEUMATISM

416. **Untoward Effects of Phenylbutazone (Butazolidin) —a Re-evaluation**

I. L. SPERLING. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] **2**, 203–211, June, 1959. 26 refs.

The results of phenylbutazone therapy in 590 adult patients (aged 19 to 75 years) suffering from various rheumatic disorders are reported. The daily dose ranged from 100 to 800 mg., the average daily maintenance dose being 200 mg. In 54 cases treatment was given for at least one year. Excellent or good results were obtained in 34 out of 78 cases of rheumatoid arthritis, in 95 out of 115 cases of osteoarthritis, and in all 10 cases of ankylosing spondylitis. It was necessary to discontinue treatment in 30 of the 55 cases in which undesirable reactions occurred. These reactions, which were observed more frequently in patients with rheumatoid arthritis than in those suffering from other forms of rheumatism, included rashes and gastro-intestinal distress. Leucopenia developed in 2 patients. For the most part, the reactions occurred within the first month of treatment and when the daily dose exceeded 300 mg.

In view of these results the author recommends that phenylbutazone should be administered with caution in cases of heart disease. Fluid retention must be avoided, especially in the elderly, and for this purpose the dosage of the drug must be low and any gain in weight must be checked. The drug must not be given on an empty stomach. Antacids may be of use if mild gastro-intestinal symptoms develop. The amount of salt in the diet should be restricted in all cases. Phenylbutazone therapy is contraindicated in patients with a history of peptic ulcer. During the early stages of treatment a complete blood count is performed weekly; later, the blood is examined at intervals of 4 to 6 weeks. The patient is warned to report immediately the occurrence of untoward signs and symptoms such as pruritus, rash, sore throat, fever, gastro-intestinal disturbances, and tarry stools. The author considers that when these precautions are observed long-term therapy with phenylbutazone is likely to prove both safe and effective in the management of rheumatoid arthritis, ankylosing spondylitis, and other chronic forms of rheumatism.

A. Garland

417. **The Mucocutaneous Lesions of Reiter's Syndrome**

M. M. MONTGOMERY, R. M. POSKE, E. M. BARTON, D. T. FOXWORTHY, and L. A. BAKER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **51**, 99–109, July, 1959. 6 figs., 6 refs.

The incidence of mucocutaneous lesions in 38 patients with Reiter's syndrome seen at the Veterans Administration Hospital, Hines, Illinois, was 80%. The commonest site was the glans penis, which showed perimeatal erosions and balanitis circinata. These lesions are not influenced by antibiotics or corticosteroids. In view of the high incidence of mucocutaneous involvement it is suggested that Reiter's syndrome in its complete form might better be regarded as a tetrad consisting of urethritis, conjunctivitis, arthritis, and mucocutaneous lesions.

G. W. Csonka

418. **Hyperostotic Discosomatic Vertebral Arthrosis.** (Artrosi disco-somatica iperostosante vertebrale)
A. ROBECCHI. *Minerva medica* [*Minerva med. (Torino)*] **50**, 2125–2137, June 27, 1959. 13 figs., 8 refs.

The condition first described by Forestier and Rotes-Querol (*Ann. rheum. Dis.*, 1950, **9**, 321; *Abstr. Wld Med.*, 1951, **9**, 641) as senile ankylosing hyperostosis of the spine, but which the present author prefers to call hyperostotic discosomatic vertebral arthrosis, has received little attention in the literature of rheumatism. In the opinion of the author many cases escape diagnosis even after radiological examination, so that errors occur both in prognosis and in treatment, while some cases have even found their way into the literature labelled ankylosing spondylitis.

Figures are quoted to show that the condition is commoner than is generally supposed. It occurs especially in older patients, and occupational and family history have little bearing on the diagnosis, which is often made by chance on the basis of a radiograph taken for some other purpose. The level and extent of spinal involvement vary widely. The characteristic bony lesion occurs most commonly in the thoracic region, particularly on the right side. Peripheral joints and bony surfaces far from joints may also be affected. Because the disease so often attacks the aged, kyphosis is not necessarily significant. Local or generalized pain or stiffness are the commonest symptoms. Although the bony lesion is usually thoracic, yet it is in the lumbar region that the patient usually feels the pain, which is often aggravated by movement or prolonged standing, is most obvious first thing in the morning, and tends to pass off as the day wears on. Rest in the horizontal position reduces and may abolish it. Unlike that of inflammatory spinal disease the pain of this condition does not occur at night, and it is never referred remotely. Physical examination may be no more informative than the history. Forced movement of the spine sometimes increases the pain, but tenderness on pressure over the spinous processes or near the transverse processes is rare. There is often some stiffness in peripheral joints such as the hip and shoulder. In a series of more than 20 cases [exact number not stated] seen at the Turin Rheumatological Centre the author was unable to confirm the occurrence of psychiatric disturbance, such as depression, described by other authors. Haematological changes, such as raised erythrocyte sedimentation rate (E.S.R.), and circulatory disorders, such as hypertension, were notably absent. Diagnosis may be possible only by radiography. The characteristic appearance is of new bone formation which appears to have "dripped" down the right half of the thoracic spine. Protrusion of the intervertebral disks may enforce a convex, bridge-like appearance on the new bone as it crosses the intervertebral spaces. Arthritis may affect the various intervertebral joints and there may be osteophyte formation. The normality of the sacro-iliac joints is important in the differential diagnosis from ankylosing spondylitis, which also occurs at an earlier age and may be associated with systemic symptoms and a raised E.S.R.

The symptoms are frequently mild or absent and the outlook good. The organic changes show no regression, yet the symptoms are intermittent and intervals of freedom may last for months or even years. Rest is important in the relief of pain, as also are antirheumatic and analgesic drugs. The author gives first place in treatment to phenylbutazone, provided there are no contraindications. Aspirin may also help, but steroids are useless. Any physiotherapy must be determined by the needs of the individual case.

The author sets out the various views as to the origin and nature of the disease: that it is a link between ankylosing spondylitis and rheumatoid arthritis; that it is due to metaplastic ossification of the anterior longitudinal ligament; that it is a normal component of the ageing process; and that it is a separate disease. He himself belongs to a school that sees it as a form of spinal arthritis. He finds it difficult to account for the anatomical localization and examines various theories.

A. C. F. Green

419. **Clinical Research on the "Rheumatoid Factor".** (Ricerche cliniche sul "fattore reumatoide")
M. GIORDANO, M. ARA, and E. DRAMMIS. *Riforma medica* [*Rif. med.*] **73**, 783–788, July 11, 1959. 11 refs.

In this paper from the Medical Clinic of the University of Naples the authors first review the evolution of the various tests for the detection of the rheumatoid factor in human serum. They then report their own experience with the "R.A." test, a modification of the latex fixation test of Singer and Plotz, in 30 cases of rheumatoid arthritis, 3 of ankylosing spondylitis, 40 of painful osteoarthritis, and 188 of non-rheumatic disease, including 133 cases of diabetes and 5 of Addison's disease. The result of the test was positive in 96·7% of cases of rheumatoid arthritis, whereas in acute rheumatism it was positive in 2% of cases only. On the other hand positive results were obtained in 25% of the cases of painful osteoarthritis, in 27·7% of the cases of diabetes, and in 4 of the 5 cases of Addison's disease. The authors conclude that the R.A. test is useful in the diagnosis of rheumatoid arthritis, though the possibility of false positive reactions has to be borne in mind, especially in cases of painful osteoarthritis, in which the problem of differential diagnosis often arises. The R.A. test is slightly more sensitive and is easier to carry out than the Rose–Waaler test.

E. Forrai

420. **Clinical and Pathological Study of Polyneuritis Arising during the Course of Rheumatoid Arthritis.** (Étude anatomo-clinique des multinévrites au cours des polyarthrites chroniques évolutives)
J. GRAVELEAU, F. DEMAISON, and M. MORIN. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **35**, 2080–2090, June 18, 1959. 7 figs., 48 refs.

In view of the rarity of neurological complications in rheumatoid arthritis the authors report 2 further cases seen at the Hôpital Foch, Suresnes, Paris, in which polyneuritis due to periarteritis nodosa was present as a complication of rheumatoid arthritis. Both occurred in women aged 64 in whom the rheumatoid disease had existed for 11 and 4 years respectively. Both had received courses of gold therapy in the past and more

recently treatment with prednisone. Fever accompanied by generalized pain was noted in both cases. There was a leucocytosis of 15,000 per c. mm., with a preponderance of polymorphonuclear leucocytes, in one case and of 18,960 per c. mm. in the other. The neurological signs included paralysis or paresis of the extremities, with absent tendon jerks, and hypoaesthesia of the hands and feet; in addition there was exquisite tenderness on compressing the muscles. Muscle biopsy examination performed in both cases demonstrated periarteritis nodosa affecting the arterioles. One patient died and at necropsy widespread foci of periarteritis were found. The other recovered, but the neurological signs showed little change and gangrene developed in one toe.

The authors present an extensive review of the literature in which previous similar cases have been reported. In most the signs and symptoms were as described above, and a history of gold, copper, or steroid therapy was common, particularly the last in the more recent cases. Neurological signs, usually symmetrical, generally affect the extremities, but rarely the distribution of the cranial nerves. Post mortem the arterial lesions are found to be widespread and have been demonstrated in the heart muscle and valves, spleen, intestine, kidney, and the nutrient arteries of peripheral nerves. The treatment of such cases is extremely difficult, involving as it does the cessation of steroid therapy with the risk of serious withdrawal symptoms. These patients have often been receiving high doses of steroids and their too rapid withdrawal has been known gravely to increase the extent of the paralysis. In the authors' opinion the treatment of these neuropathies can only be prophylactic, meaning thereby that steroids should be prescribed only in exceptional cases of rheumatoid arthritis and then in low dosage. *William Hughes*

421. **The Comparative Effects of Phenylbutazone and G27202 (Metabolite I) in Patients with Rheumatoid Arthritis: an Assessment of Methods for Antirheumatic Drug Evaluation**

P. P. VAUGHN, D. S. HOWELL, and I. M. KIEM. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] **2**, 212–223, June, 1959. 5 figs., 13 refs.

For various periods during an investigation lasting 12 weeks 24 adult patients with rheumatoid arthritis were given aspirin, a placebo, phenylbutazone, and Metabolite I, a derivative of phenylbutazone. The last two drugs were given in doses of 800 mg. on the first day and 600 mg. on the second day; subsequently the dose was maintained at 400 mg. daily. Observations were controlled by administering the drugs in the form of a white powder in gelatin capsules of identical appearance. Throughout treatment special note was made of any changes in joint swelling, degree of tenderness, pain, morning stiffness, fatigue, speed of walking, and grip.

Apart from salt and water retention during the early phases of treatment there were no important side-effects from administration of Metabolite I. The response to this drug was at least equal to the response obtained with phenylbutazone. During Metabolite-I therapy there was highly significant improvement in grip and in the duration of morning stiffness. On the other hand equivocal results were obtained with completely objective measurements such as the erythrocyte sedimentation rate and joint circumference. Altogether an excellent or a good response was obtained in 12 cases.

A. Garland

422. **Corticosteroid Therapy in Rheumatoid Arthritis: Comparative Study of Effects of Prednisone and Prednisolone, Methylprednisolone, Triamcinolone, and Dexamethasone**

D. H. NEUSTADT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 1253–1260, July 11, 1959. 15 refs.

At the Arthritis Clinic of the University of Louisville 65 patients (39 female and 26 male) with rheumatoid arthritis were treated with prednisolone or prednisone, methylprednisolone, triamcinolone, or dexamethasone. Since no difference has been reported in the literature between prednisone and prednisolone, these two preparations are grouped together as "prednisteroids". The patients' ages ranged from 23 to 71 years and the average duration of the disease was 7 years. Each patient was classified in respect of severity of the disease and functional disorder according to the criteria of the American Rheumatism Association, 31 patients being in Stages 3 and 4 (moderately advaneed and advanced). None of the patients had received antimalarials or gold therapy within one year of starting treatment with corticosteroids, although all had received salicylates and "basic therapy". A clinical evaluation of each patient was performed "at regular and frequent intervals". Certain laboratory studies were carried out periodically, including estimation of the haemoglobin level and haematocrit, total and differential leucocyte counts, erythrocyte sedimentation rate, total plasma protein and albumin and globulin levels, and urinary sugar and albumin content.

In 48 cases prednisteroids were given for an average period of 2 years. Methylprednisolone was given to 39 patients, of whom 32 had previously received long-term prednisteroid therapy, and 25 received triamcinolone before or after the methylprednisolone, while in 7 cases methylprednisolone was the only corticosteroid given. Triamcinolone was given to 38 patients, of whom 31 had received prednisteroids and 25 were given methylprednisolone either before or after the triamcinolone, triamcinolone being the only corticosteroid given in 7 cases. A firm maintenance dose of each corticosteroid was established before another was substituted. Patients served as their own controls without the administration of placebos as soon as the early part of the study was finished. This method of comparison was preferred to the double-blind method, mainly because of the dangers of interrupting corticosteroid treatment. Altogether 25 patients received prednisteroids, triamcinolone, and methylprednisolone for sufficiently long periods to allow comparative analysis of the results. The remaining 40 patients did not receive all these corticosteroids and are therefore not included in the analysis. On the other hand 40 patients were later given dexamethasone, enabling a preliminary comparison of the effects of this and other corticosteroids to be made.

Comparable antirheumatic effects were obtained with all compounds in the majority of cases. The average daily maintenance doses were: prednisteroids, 11·4 mg.; triamcinolone, 7·8 mg.; methylprednisolone, 8·12 mg.; and dexamethasone, 1·4 mg. The laboratory investigations revealed no consistent difference between the various corticosteroids except that glycosuria and an increase in the blood sugar level occurred more often with the prednisteroids than with the other preparations. The side-effects occurring in the 25 patients who received adequate treatment with prednisteroids, methylprednisolone, and triamcinolone are listed. The incidence of the expected manifestations of hypercortisonism and of peptic ulcer and other gastro-intestinal symptoms was similar with all compounds. Emotional disturbances, oedema, and glycosuria occurred most often with the prednisteroids and ecchymotic and purpuric skin manifestations with methylprednisolone. Two "new" side-effects are reported as occurring almost exclusively with triamcinolone, namely, "hot flashes", erythema of the face and increased perspiration, and, more serious, muscle weakness accompanied by loss of weight, which occurred in about 24% of patients receiving this steroid. In contrast dexamethasone had a remarkable appetite-stimulating effect and produced a striking gain of weight.

None of the steroids was outstandingly superior to the others in clinical effect and freedom from side-effects. The author concludes that methylprednisolone is probably the steroid of choice for initial treatment, but dexamethasone may prove useful for the early treatment of the underweight patient with rheumatoid arthritis.

J. Warwick Buckler

423. **Radiological Changes in the Bones in Juvenile Rheumatoid Arthritis and Their Reversibility.** (Über röntgenologische Knochenveränderungen bei primärchronischer Arthritis im Kindesalter und ihre Rückbildungsfähigkeit)

H. SPIESS. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **107**, 317–322, July, 1959. 12 figs., 20 refs.

This study of 3 children with Still's disease, in each of whom it took a different course, is reported from the University Paediatric Clinic, Göttingen. Although the disorder is generalized, the bones consistently tend to become demineralized and osteoporotic, and this tendency is believed to be aggravated by the modern use of ACTH (corticotrophin) and steroids, which do not necessarily arrest the disease process. The administration of vitamin D helps to counteract the tendency to demineralization, but unfortunately it also diminishes the beneficial effects of the hormones. For this reason the author suggests that the vitamin should not be given unless osteoporosis is marked; if it is given its administration should be accompanied by prompt reduction in the dosage of steroids, or they may be given intermittently, or better still completely omitted. Radiologically, in all 3 of the author's cases some of the changes in the bones were subsequently reversed, but it is stressed that orthopaedic measures and long-term physiotherapy form an integral and essential part of the treatment. [There is no indication of the dosage of vitamin D or the type of preparation employed.]

D. Preiskel

424. **Ankylosing Spondylitis: Results of Treatment, and Their Presentation**

D. O'CONNELL. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **10**, 156–157, July, 1959. 1 ref.

The results obtained with radiotherapy in 87 cases of ankylosing spondylitis seen at Charing Cross Hospital, London, are described. A single course of treatment was given, with a dosage of 600 to 700 r. to the bone marrow and an integral dose of 5 to 7·5 mg./r. This was supplemented by physiotherapy and when necessary for associated depression by psychotherapy.

The cases were classified according to the severity of the disease before and the degree of remission after treatment. Of the 87 patients, 75 were in remission or had made a complete recovery after 3 months' treatment; of 74 followed up after 5 years, 36 were in remission. Patients with a mild form of the disease appeared to respond more completely and more consistently to radiotherapy.

M. Wilkinson

425. **Procto-colitis and Other Pelvic Infections in Relation to Ankylosing Spondylitis, with a Note on the Vertebral Venous System**

R. G. GRAINGER. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **10**, 138–150, July, 1959. 17 figs., bibliography.

In this paper from St. Thomas's Hospital, London, the author discusses the evidence for the view that pelvic infection may precipitate ankylosing spondylitis in susceptible subjects and describes 7 new cases of ulcerative colitis with sacro-iliitis or classic ankylosing spondylitis. In 6 of the cases in which the history was adequate the arthritis began within 3 years of the onset of colitis. He points out that a review of the literature suggests that the association of these diseases is too frequent to be due to chance. He also briefly refers to 2 cases of Crohn's disease with bilateral sacro-iliitis. The progression of Reiter's syndrome to ankylosing spondylitis is illustrated in 3 case histories. The sacro-iliac arthritis of Reiter's syndrome may be more frequently unilateral, but is otherwise difficult to distinguish from ankylosing spondylitis. The sacro-iliac and spinal changes in paraplegia are described and their possible relationship to chronic urinary infection is discussed. Involvement of the sacro-iliac joints in rheumatoid arthritis is considered to be uncommon and never a dominant feature of the clinical picture.

There is evidence in the literature which suggests that prostato-vesiculitis is frequent in patients with ankylosing spondylitis, and the thesis that pelvic infection may cause non-suppurative bone lesions is supported by the findings in 2 cases—one with bilateral sacro-iliac changes after a septic abortion and one with osteitis pubis and ischii following post-prostatectomy sepsis.

Discussing the vertebral venous system the author suggests that through this channel pelvic infection may cause sacro-iliac changes which in genetically predisposed patients may herald the development of classic ankylosing spondylitis. [He does not attempt to explain the occurrence of peripheral arthritis in this condition.]

M. Wilkinson

Physical Medicine

426. **Response to Stretch of Hypertonic Muscle Groups in Hemiplegia**

J. B. BRENNAN. *British Medical Journal* [*Brit. med. J.*] 1, 1504–1507, June 13, 1959. 44 refs.

The author of this paper from St. James's Hospital, London, states that a chance observation appeared to indicate that the spasticity of certain muscle groups in residual hemiplegia could be abolished by subjecting the spastic muscles to long periods of stretch. A controlled trial of prolonged stretch as a therapeutic measure was therefore carried out on 14 patients in whom the onset of hemiplegia had been sudden and was presumably of cardiovascular origin, the duration of the hemiplegia was more than 6 months, and no lessening of tonus or increase in active movement had been noted for 4 weeks or longer.

An affected flexor group of elbow, wrist, or finger muscles held contracted by tonic spasm was stretched by splinting the limb in extension at the corresponding joint. The most satisfactory appliance was a light-weight, well-padded polythene–polyurethane splint; plaster of Paris was tried, but was discarded because of its tendency to erode the skin. Splinting was maintained for about 3 months, the splint being removed only twice a day for washing and exercising the limb; once spasm had been abolished the splint was worn for shorter and shorter periods and finally discarded.

The changes in the treated muscle groups were compared with those in affected but untreated flexor and extensor groups controlling a neighbouring joint. In every case the treated muscle groups showed a much greater improvement than the controls. Decrease in flexor muscle tonus was demonstrated by the fact that, starting from a position of full flexion, the arc of passive extension during which no resistance could be felt progressively increased. Commonly the amount of this increase was such that the limb could be fully extended without resistance. Of the 14 patients, 6 retained normal tonus in the treated muscle group and a degree of voluntary extension for an average of 58 weeks after stretching was stopped; in 4 patients the muscles reverted to their original state within this time. In the former group the intensity of hypertonus before treatment was moderate, and in the latter group it was marked; the periods of constant and intermittent stretch were longer in the former group. It is suggested that for moderate spasm 12 weeks' constant and 8 weeks' intermittent stretch are required. The remaining 4 patients in the series died from various causes. Very little change was observed in the control muscle groups. The author states that if a patient was able to grip fairly firmly, then active extension at all joints of the upper limb could be obtained by this treatment; if, however, the grip was absent or feeble there was no useful recovery of active extension.

Kenneth Stone

427. **Abbreviated Electrodiagnostic Tests of Denervation: a Comparative Study**

L. D. AMICK and R. P. HICKEY. *Annals of Physical Medicine* [*Ann. phys. Med.*] 5, 48–56, May, 1959. 2 figs., 5 refs.

The normal technique of plotting an intensity–duration curve as a measure of neuromuscular excitability may be abbreviated by observing the intensities required to produce stimulation at two stated durations only and determining the ratio between them. Because of the ease and speed of this technique it is being increasingly employed. Less extensively used is the determination of the progressive current ratio, using a slowly rising (triangle-shaped) stimulus as a test for denervation.

This paper from the Royal Free Hospital, London, and the R.A.F. Medical Rehabilitation Unit, Chessington, Surrey, describes an attempt to estimate the magnitude of the error inherent in these quick techniques, and is based on a series of examinations of normal, partially denervated, and totally denervated muscles in patients with peripheral nerve injuries and chronic neurological conditions. The constant current (C.C.) ratio was the ratio of the threshold intensity of contraction with a 100-millisecond square-pulse stimulus to that with a one-millisecond square-pulse stimulus. For the constant voltage (C.V.) ratio the stimuli required for threshold contraction at 100 milliseconds and 0·1 millisecond were used, while the progressive current (P.C.) ratio was that between the intensities necessary with a triangular-pulse (slowly rising) stimulus, that is, ascending in 1·5 second and decaying in one second, and a square pulse of 100 milliseconds duration.

In the examination of normal muscles C.C. ratios above 2 were recorded in 5·2% of the tests and C.V. ratios above 2 in 3·4%. Partially denervated muscles gave a C.C. ratio less than 2 in 7·9% and a C.V. ratio less than 2 in 7·0% of the tests. No completely denervated muscle gave a C.C. or C.V. ratio of less than 2·5. The P.C. ratio was between 1·1 and 2·1 in most tests on normal and denervated muscles; apart from the fact that there was much overlap of results, intolerance of the patient to the procedure also reduced the practical value of this study.

The authors conclude that their results emphasize the importance of using these abbreviated techniques only in conjunction with other diagnostic methods, such as electromyography, if error is to be avoided.

B. E. W. Mace

428. **Physiological Hazards of Microwave Radiation: a Survey of Published Literature**

H. KALANT. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **81**, 575–582, Oct. 1, 1959. Bibliography.

Neurology and Neurosurgery

429. **Familial Spastic Paraplegia with Amyotrophy, Oligophrenia, and Central Retinal Degeneration**
K. KJELLIN. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **1**, 133–140, Aug., 1959. 4 figs., 32 refs.

An apparently new clinical entity found in two pairs of brothers is described. The material is too limited to permit definite conclusions on the heredity, but it seems probable that there is a recessive heredity with an underlying simple gene anomaly. The different parts of the syndrome are as follows: (1) Nonprogressive mental retardation. (2) Spastic paraplegia, with onset of symptoms at about 25 years of age and with rather slow progress. (3) Slowly progressing amyotrophy, due to a peripheral neurogenic lesion, with atrophy of the small hand muscles and, in 2 cases, of the leg musculature. The hand muscle atrophy seems to become apparent at about 35 years of age. (4) Characteristic central retinal degeneration with small atrophic foci and pigment displacement in the macula and its immediate vicinity. The eye changes probably have a late onset and seem to progress rather slowly.—[Author's summary.]

430. **A Clinical Aphorism in the Diagnosis of Multiple Sclerosis**
F. R. FERGUSON and L. A. LIVERSEDGE. *Lancet* [*Lancet*] **1**, 1159–1160, June 6, 1959. 3 refs.

The authors have noted that in some patients with disseminated sclerosis signs may outstrip symptoms in a way rarely if ever seen in other neurological disorders. They consider that the syndrome of frank pyramidal signs in both legs and symptoms in one leg only is a very significant pointer to a diagnosis of disseminated sclerosis. In this paper from the University of Manchester they state that they have now observed some 30 cases and that in none was the diagnosis proved incorrect in the light of subsequent developments. For this clinical picture they use the term " aphoristic multiple sclerosis ".
I. Ansell

431. **Syringomyelia in Children.** (Сирингомиелия у детей)
G. L. OSTAPOVIČ. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **59**, 847–851, No. 7, 1959. 3 refs.

Syringomyelia in children is not so uncommon as has been believed. Kryshova *et al.* described 7 cases in children aged between 20 months and 15 years, and the present author now reports 9 cases in patients aged from 10 to 15 years, 5 of whom were attending the Physical Culture Clinic at Voronezh for scoliosis. Of the 9 children, 2 also had symptoms of syringobulbia. Signs leading to the diagnosis were scoliosis (present in 8 cases), deformities of the thoracic cage (4), and Horner's syndrome (4); facial hemiatrophy, vasotrophic and sensory motor disturbances in the upper limbs and trunk manifested by cyanosis of the hands, persistent furunculosis, hyperhidrosis, muscular atrophy, and vague pains were also noted. There was hypoaesthesia to pain and temperature of segmental or patchy distribution, painless burns being not uncommon. In addition to these 9 children the author also found among 100 adult cases of the disease 11 who gave a history dating back to childhood. He points out that symptoms at this early age are usually mild and liable to be missed by the clinician. Difficulty in writing led to several of his child patients having to abandon schooling and take up labouring work of an unsuitable character.

The opportunity to confirm the diagnosis pathologically was naturally rare, but in 2 cases subjected to Pussep's operation large cavities were found in the cervical enlargement of the cord, from one of which 30 ml. of fluid was withdrawn. These experiences have led the author to the conclusion that syringomyelia is a disease in which abnormalities of the medullary tube are associated with an increase in spongioblasts, and he quotes the opinion of Margulis that hydromyelia and gliomatosis are manifestations of one and the same pathological process. Pure forms of hydromyelia are rare, but in children this form predominates. The disease should be suspected in patients with scoliosis due to no obvious cause and in children with the signs and symptoms in the upper extremities described above. If the possibility of syringomyelia cannot definitely be excluded, these children should be given suitable work of a light nature and careful supervision exercised to avoid possible traumata. If the presence of the disease is confirmed radiotherapy and other therapeutic measures may be tried.
L. Firman-Edwards

BRAIN AND MENINGES

432. **Pubertas Praecox as a Symptom of Cerebral Disease.** (Преждевременное половое созревание как симптом поражения головного мозга)
JA. B. CIMMER. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **59**, 868–871, No. 7, 1959. 3 figs.

In patients with pubertas praecox it occasionally happens that exhaustive investigation of the endocrine system fails to reveal any abnormality. The present author has observed 7 such cases, in some of which a severe lesion of the midbrain was later demonstrated, and in this paper describes 3 of them in detail.

The first showed abnormal sexual development with adolescent voice changes at the age of 3, but no mental retardation; the patient died at 4½ years of tuberculous colitis. At necropsy no endocrine lesion was demonstrable, but a tumour measuring 3·5 by 2·3 cm. was found in the region of the tuber cinereum; histologically it was composed of fibrous tissue and glioma cells. Internal and external hydrocephalus was also present. The

second patient developed rapid enlargement of the sexual organs with growth of pubic hair at the age of 2½, and at age 8 his stature, appearance, and bone development were those of a boy of 14, but his dentition was in accordance with his true age. At this stage he developed generalized epileptiform attacks. This patient's intellect was obviously retarded. He died at the age of 16 from pneumonia, and necropsy revealed a glioma just behind the optic chiasma, with external hydrocephalus. The third patient, a female, had suffered cerebral trauma at 6 months. At age 8 she began to show excessive growth and sexual precocity, and at 9 she had the appearance of a girl of 14 or 15. Simultaneously she began to manifest symptoms of petit mal, and a year later developed epileptiform convulsions with loss of consciousness and also showed obesity and intellectual impairment. This patient is still alive and suffers from attacks of petit mal and occasionally grand mal; she is self-centred, introspective, and liable to affective outbursts, but is generally sluggish. Pneumoencephalography revealed sharp configuration of the lateral ventricles, but poor outline of the cisterna basalis. She suffers from severe headaches, which are often accompanied by vomiting and followed by convulsions.

It is concluded that pubertas praecox may develop as a result of injury, tumour, or other lesion of the hypothalamus or midbrain and may occur in the absence of endocrine dysfunction. In such cases (1) it is preceded by cerebral symptoms such as epileptiform seizures or intellectual deterioration, (2) the precocious development of the sexual organs is not necessarily accompanied by progressive increase in general growth or by mental precocity, and (3) the dental formula corresponds to the chronological age of the child. *L. Firman-Edwards*

433. **Psychical Disturbances Caused by Tumours of the Third Ventricle.** (Les troubles psychiques produits par les tumeurs du troisième ventricule)
C. Arseni and I. Opresco. *Encéphale* [*Encéphale*] **48**, 235–245, 1959. 2 figs., 15 refs.

It is well known that the psychical disturbances which appear during the evolution of a cerebral tumour bear a relation to the site of the lesion and the degree of intracranial pressure, but it is less well known that tumours in the region of the third ventricle may produce mental disturbance before increased pressure develops. In this report from the Neurosurgical Clinic, Bucharest, the authors discuss 28 cases of tumour of the third ventricle, in 9 of which there was no mental disturbance, but in 19 considerable disturbance; among these last intracranial pressure was increased in 10 cases, but in 9 it was not.

The first symptom to appear is usually a diminution of activity and a slowness of reaction. A little later there is a defect of attention and perception, with some loss of memory. The patient becomes more and more isolated from his surroundings, disorientated, neglectful, confused, and often somnolent. Occasionally he may be agitated, and the authors report one case in which transient hallucinations occurred. There appears to be no definite relationship between the pattern of psychical symptoms and the exact site of the tumour in relation to the third ventricle. The syndrome resembles in general that produced by frontal-lobe lesions, with no neurological signs or only very slight bilateral signs. The mental changes may appear before there is any sign of increased intracranial pressure. The authors speculate on whether the mental disturbances are caused by interference with corticodiencephalic pathways.

J. MacD. Holmes

434. **The Dangers of Treatment with Anti-epileptic Drugs, with Special Reference to Severe Side-effects Reported in the Literature and Observed Personally.** (Therapieschäden durch antiepileptische Mittel unter besonderer Berücksichtigung schwerer Nebenwirkungen an Hand der Literatur und eigener Fälle)
R. Dreyer. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **27**, 401–423, July, 1959. Bibliography.

This is a most valuable survey of material concerning the complications and side-effects of treatment with anticonvulsive drugs collected from the international literature and illustrated by examples drawn from the author's own experience at the famous Bethel Hospital, with its large numbers of epileptics. Reported cases of fatal complications of treatment with hydantoin, methoin, troxidone, and phenacemide are listed and the dangers of each drug are fully discussed. Much sound advice is offered for avoiding such complications.

W. Mayer-Gross

435. **An Evaluation of Orphenadrine Hydrochloride (Disipal)**
S. Rosenfeld and M. G. Goldner. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **7**, 502–507, June, 1959. 3 refs.

At the Jewish Chronic Disease Hospital, Brooklyn, New York, orphenadrine hydrochloride ("disipal") was given to 21 patients with severe Parkinsonism who had failed to respond to other forms of treatment. Of these 21 patients, 12 suffered from post-encephalitic Parkinsonism, 5 from the idiopathic form of the disease, and 4 from the arteriosclerotic form. The drug was always given in combination with other agents, the dosage being 150 mg. daily. The only toxic effects observed were difficulty in micturition and nausea in 2 patients.

The drug was effective in relieving rigidity in 11 of the 21 patients, reducing sialorrhoea in 10 out of 18 patients, and improving depression in 12 out of 16. Oculogyric crises were prevented in 2 out of 9 patients in the post-encephalitic group. The drug had no influence on tremor. In an addendum to the paper the authors state that orphenadrine citrate in a dosage of 100 mg. twice daily proved to be highly effective, giving even greater relief of rigidity.

[Although the authors have, in fact, given orphenadrine hydrochloride in conjunction with other agents in 125 cases of severe Parkinsonism, they report the results obtained in only 21 of these patients. The clinical trial as presented is therefore of limited value in evaluating the efficacy of this drug.] *A. G. Freeman*

Psychiatry

436. **Mother–Child Separation and Delinquency**
S. NAESS. *British Journal of Delinquency* [*Brit. J. Delinq.*] **10**, 22–35, July, 1959. 17 refs.

The hypothesis of Bowlby (*Maternal Care and Mental Health*, Geneva, 1952), namely, that prolonged separation from the mother or mother substitute during the first 5 years of life " stands foremost among the causes of delinquent character formation ", is discussed.

Delinquent character has to be distinguished from delinquent acts without abnormality of personality. The present author uses a working definition, regarding as delinquents only those who show at least two of the following: stealing, playing truant, violent behaviour, unruliness, running away, or staying out late. Such behaviour is presumably correlated with the deeper character traits intended by the term " delinquent character formation ".

It is pointed out that a proven association between these symptoms and separation from the mother does not establish this factor as a prime cause of delinquency. Families that are deficient in other respects, through low mentality, poverty, parental discord, or poor social standards, are the ones most likely to part with their children. Sutherland holds that delinquents are normal in character development and that their behaviour simply conforms to the expectations of the group to which they belong. Even if there is a difference in character formation between delinquents and non-delinquents it could be held that this is due to the economic and social instability of the group prone to separations rather than to the fact of separation itself. It could be the periods they spend with their unsatisfactory families rather than the periods of separation that are responsible for the delinquents' characters. The work of Goldfarb suggests that permanent separation from the mother at a very early age, although such separation may produce other adverse psychological characteristics, does not lead to delinquency.

In order to distinguish between these interpretations the author compares the records of a group of delinquent boys (defined as above) taken from the files of the Oslo Protection Council with those of their non-delinquent brothers. The factor of family environment is thus held constant. It was found that 4 delinquents and 8 non-delinquent brothers (10% and 20% respectively) had been separated from their mothers for at least 6 months before the age of 5; also that 6 delinquents and 11 non-delinquents (15% and 27% respectively) had been separated for at least 3 months. The separations were, therefore, less frequent among the delinquents, which is contrary to Bowlby's hypothesis.

The author admits that the differences are too small to warrant a conclusion opposite to that of Bowlby. He points out that the method excludes consideration of the only child, who might be particularly affected by separation from his mother. He points out several differences between the sample he studied and that studied by Bowlby. Thus the latter's group of 44 young thieves were of a different nationality and had received child guidance treatment; also they may have included a higher proportion of neurotics.

D. J. West

437. **The SHP Test—an Aid in the Detection and Measurement of Depression**
R. E. PECK. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **1**, 35–40, July, 1959. 7 refs.

In this paper from the Veterans Administration Hospital, New York, the author describes a test for the diagnosis and assessment of depression based on the measurement of changes in salivary secretion. (The test derives its name, the " SHP test ", from the initials of Strongin and Hinsie, the original workers on salivary secretion in psychiatric patients, and of the present author.) Saliva is collected on 3 dental cotton-wool rolls, which are placed in the cheeks and under the tongue and left in position for 2 minutes. The increase in weight of the rolls is then accurately measured. Salivary secretion is normally higher in children and negroes than in white adults and is reduced in fever; body weight and smoking have no influence on it. Depressed patients secrete significantly less saliva than normal subjects and show a diurnal variation in the rate of secretion, which is highest in the afternoon; the degree of depression, however, seems to have no relation to the degree of reduction of secretion.

The author considers that although much remains to be done before the real value of the test can be established, the relationship between clinical depression and lowered salivary secretion is a clear one. He suggests that the test may be useful as a gauge of progress in the same way as the temperature or leucocyte count is used in infections, and that serial readings should be made during treatment with electric convulsion therapy or drugs. He makes a plea for the wider study of the SHP test.

Gavin Thurston

438. **The Salivary Curve: a Psychiatric Thermometer?**
G. F. SUTHERLAND. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **116**, 20–24, July, 1959. 12 figs., 7 refs.

In this report from the Department of Mental Hygiene of the State of Maryland the author describes methods which have been used in investigating the variations in salivary flow accompanying emotional changes. Saliva is collected by placing a suction capsule over the opening of Stensen's duct. The capsule is connected to a liquid-filled system, and minute pressure changes in the duct are readily transmitted to a rubber diaphragm. This in turn displaces drops of saline which close an electric

circuit operating a recording pen. Stimuli producing salivation are either gustatory or irritant. Reflex salivation is involuntary and prompt, and lasts long enough to allow detailed observation. Rigid attention to technical detail is vital, as responses to stimuli extraneous to the experiment are easily recorded. In the production of conditioned reflexes the stimulus used is a metronome, reinforced by the introduction of lemon juice into the mouth. A brief stimulus causes a series of spurts of saliva which diminish over about 8 minutes. The normal curve of secretion is influenced by drugs such as anaesthetics, alkaloids, and tranquillizers, while in the absence of extraneous influences the contour of the curve appears to be related to the subjective sense of well-being. A consistent change in the curve "heralds a coincident change in the internal milieu".

The author points out that anxiety in the psychiatric sense corresponds to "irritation" in the terminology of conditioned reflexes and depression to "central inhibition". Inhibition may occur in conjunction with many disorders and is not necessarily characteristic of depression. With anxiety the level of secretion is high and with depression it is low. In one case of anxiety the administration of "amytal" (amylobarbitone) restored a high secretion level to normal; in another, in which a sedative produced depression, this effect was correctly forecast by sialometry.

In the author's opinion sialometry is of no diagnostic value apart from indicating gross anxiety or depression. On the other hand changes in the internal milieu are reflected sensitively in the salivary flow, which is remarkably constant in any individual, and the method offers a promising field of investigation in which little has been published, particularly recently. The article is illustrated by pictures of apparatus and by specimen curves of salivary flow in different circumstances.

Gavin Thurston

439. **Emotional Content of Suicide Notes**

J. TUCKMAN, R. J. KLEINER, and M. LAVELL. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **116**, 59–63, July, 1959. 7 refs.

In a study of 742 deaths classified as suicide by the Office of the Medical Examiner in Philadelphia over a 5-year period it was found that in 24% of cases the suicide had left a note. Following the methods of Shneidman and Farberow (*Clues to Suicide*, New York, 1957), who regard the suicide note as the last recorded expression of the suicide's mind, the authors analysed the emotional content of these notes. Hostility to others was shown in 24% and a positive affect in 51%, while 25% were classified as neutral. In suicides over the age of 45 the neutral tone was more frequent and there was less hostility or positive affect. Hostility was more noticeable in the notes left by divorced and separated spouses. Sex had no influence.

The authors remark that in many cases suicide appears to result from a conscious rational decision. This is particularly so in the older age groups, where there is a wish for relief from worry and discomfort. They consider that the finding of positive affect in so many cases suggests that many suicidal persons could be helped towards a resolution of their problems, their positive feelings providing an important motivational force in prevention.

Gavin Thurston

440. **A Psychotomimetic Drug of the Morphinan Group.** (Über ein Phantasticum aus der Morphinangruppe)

F. SCHULTZE-GÖRLITZ. *Nervenarzt* [*Nervenarzt*] **30**, 256–262, June 10, 1959. 13 refs.

One of the antidotes used to counteract the respiratory depression caused by morphine is N-allyl-morphinan tartrate ("lorfan"). In doses of 1 to 5 mg. this substance has been shown to have a psychotomimetic action, producing effects on normal subjects very similar to those obtained with mescaline and lysergic acid diethylamide (L.S.D.). The present author reports from the University of Göttingen the results of 25 experiments carried out with this drug on 15 patients undergoing psychotherapy. He compares the intoxication produced by lorfan with other model psychoses, as well as with natural psychotic conditions such as acute schizophrenia. He does not consider that lorfan intoxication has any psychotherapeutic application. He stresses, however, that the psychotomimetic action of lorfan does not reduce its value as an antidote to respiratory depression, for which it is, of course, used in much smaller dosage.

W. Mayer-Gross

441. **Antabuse Psychoses.** (Об антабусных психозах)

I. V. STRELBČUK and A. I. VOZDIŽENSKAJA. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **59**, 668–673, No. 6, 1959.

The authors report that of 4,116 patients with chronic alcoholism treated with "antabuse" (disulfiram), 8 developed acute psychosis in the course of treatment, this occurring in 4 cases even before the disulfiram–alcohol test was made.

In this paper the histories of 4 of the patients are described in detail. The first 2 had a long history of alcoholism, and one of them also had a history of head injury. Impairment of intellect was noted in both patients, but no psychotic features. After administration of disulfiram in a dosage of 1 g. daily for 4 and 5 days respectively headache and drowsiness developed, and disulfiram was therefore withheld. However, on the 6th day from the start of treatment in one case and on the 13th day in the other the patients became confused and apprehensive and suffered from auditory hallucinations, one patient passing through stages of delirium, schizophrenia, and hypomania. Both were treated with oxygen inhalations, iron, vitamins, and "aminazine" (chlorpromazine). Recovery was complete in 20 and 25 days respectively from the start of treatment and no later relapse was reported. Neither of these patients was subjected to the disulfiram–alcohol test.

The second 2 patients also had a long history of alcoholism, and one had received a head injury 16 years previously. The first patient received 3·5 g. of disulfiram over a period of 7 days. He complained of headache, precordial pain, and dyspnoea, which were

relieved when the drug was temporarily withdrawn. On the 9th day he was given 40 g. of 40% vodka, whereupon the previous symptoms recurred, but were somewhat relieved after he had vomited. However, 3 days later he became mentally confused and hallucinated, with amnesia for recent events. Recovery took place in 10 days. A similar mental condition recurred 2 years later when this patient was given a further course of disulfiram. The second patient, who had had a head injury, received disulfiram for 4 days. He was then given 30 ml. of 40% alcohol and immediately developed breathlessness, weakness of the left arm, and mental depression, all these signs improving after some hours. Disulfiram was continued to a total of 9 g., and 6 days later the patient developed mental confusion, amnesia, and auditory hallucinations. In this case recovery was slow, but was eventually complete in one month.

The authors stress the importance of administering disulfiram in moderate dosage, particularly if there is a history of head injury. If undesirable symptoms develop the drug should be withheld for some days. The psychotic manifestations described above are regarded as a toxic phenomenon. *Margot G. Dunlop*

PSYCHOSOMATIC MEDICINE

442. **Psychological Variables and Human Cancer: a Cross-validation Study**
A. KRASNOFF. *Psychosomatic Medicine* [*Psychosom. Med.*] **21**, 291–295, July–Aug., 1959. 4 refs.

This investigation of the association between psychological factors and the predicted survival time in malignant disease was undertaken at Washington University School of Medicine, St. Louis, in an attempt to cross-validate the results of a previous similar study reported by Blumberg *et al.* (*Psychosom. Med.*, 1954, **16**, 277; *Abstr. Wld Med.*, 1955, **17**, 60). This earlier study, in which the Verbal Scale of the Wechsler–Bellevue test (Form 1), the Minnesota Multiphasic Personality Inventory (M.M.P.I.), and the Rorschach test were used, had led to the conclusions that (1) age, education, marital status, socio-economic level, occupation, and verbal-scale intelligence score did not differentiate between patients with a short and those with a long life expectancy, but that (2) the M.M.P.I. and Rorschach test did so distinguish between these two groups.

In the present study 22 patients (11 male and 11 female) suffering from malignant melanoma were subjected to the above-named tests and similar data as to personal status recorded. They were divided into two groups of 6 and 16 patients respectively on the basis of epidemiological criteria of "fast" and "slow" progression of the tumour derived from a study reported by Nathanson and Welch (*Amer. J. Cancer*, 1937, **31**, 598). It was found that patients with "fast" progression differed from those with "slow" progression of the tumour in being of lower intelligence and lower socio-economic status, and that in contrast to the finding of Blumberg *et al.* the M.M.P.I. and Rorschach test failed to discriminate between the two groups. It is concluded that the present study [in many ways a methodologically sounder one] did not support the previous findings.
A. Balfour Sclare

443. **An Experimental Investigation of Sexual Symbolism in Anorexia Nervosa Employing a Subliminal Stimulation Technique: Preliminary Report**
H. R. BEECH. *Psychosomatic Medicine* [*Psychosom. Med.*] **21**, 277–280, July–Aug., 1959. 3 refs.

In an experimental study undertaken at the Institute of Psychiatry, London, to confirm or otherwise the psychodynamic hypothesis that libidinal conflicts are of specific significance in anorexia nervosa the postulated symbolic association between food and sexuality was investigated by means of a technique of subliminal verbal stimulation. It was considered that the hypothesis would be supported by the occurrence of more "food" responses in relation to "sex" stimuli than to "non-sex" stimuli. The subject was a 27-year-old unmarried woman suffering from anorexia nervosa and the apparatus consisted of a tape-recording of 30 words, of which 25 were "neutral" and 5 had a sexual connotation, these being preceded on the tape by a tuning series of 50 tones at 1,000 c.p.s. and of a volume of 5 db. above the average for the words; immediately preceding each word a warning tone at 1,000 c.p.s. and 10 db. above the average for the words was heard. In performing the test the patient adjusted the volume control so that the series of tuning tones could just be heard; thus the words themselves were then truly subliminal. On hearing the warning tone which preceded each word the subject wrote down, in the manner of free association, the first word that occurred to her. The recording was played over 3 times in succession, giving a total of 75 neutral words and 15 sexually significant words.

The results indicated that the "sexual" words more often (6 times out of 15) evoked a "food" response than did neutral words (11 times out of 75). The author is careful to state that caution is required in interpreting this finding for several reasons; for example, this patient may have been "conditioned" by her previous rather extensive psychotherapy to associate libidinal conflicts with orality. The results, however, lend general support to the hypothesis advanced, and suggest that the method described might with advantage be exploited in the testing of similar clinical postulates.
A. Balfour Sclare

444. **Obesity and the Denial of Hunger**
A. STUNKARD. *Psychosomatic Medicine* [*Psychosom. Med.*] **21**, 281–289, July–Aug., 1959. 7 figs., 6 refs.

In an investigation of the association between gastric motility and the experience of hunger carried out at the University of Pennsylvania, Philadelphia—the study having been prompted by the observation that 2 obese women denied feeling a sense of hunger in spite of the presence of gastric hunger contractions—the gastric motility pattern in 17 obese women was compared with that in 18 non-obese women, the two groups being comparable in respect of age, race, educational status, social class, and in their lack of previous experience of gastric intubation. In each case after an overnight fast a

Levin tube was passed into the stomach, an attached balloon inflated to a pressure of 15 cm. of water, and the gastric contractions recorded kymographically over a 4-hour period by means of a water manometer. At 15-minute intervals the subjects were questioned as to the sensation of hunger or a feeling of " abdominal emptiness " and the " desire to eat ".

The non-obese women usually reported a sensation of " hunger " during contractions of the empty stomach and of " no hunger " in the absence of contractions. Fewer of the obese women, however, reported hunger in association with gastric motility, and 5 of them never at any time experienced hunger during gastric contractions. In both groups the reports of abdominal emptiness and the desire to eat ran in parallel with reports of hunger. There was no significant difference between the obese and non-obese women regarding feelings of hunger during phases of absent gastric motility; thus the denial of hunger in the obese subjects was related to faulty discrimination during the phases of gastric contraction. Of the 17 obese women, 8 exhibited the " night-eating " syndrome, that is, morning anorexia followed by evening hyperphagia and insomnia, and in these subjects the lack of hunger during gastric motility was especially striking. The author therefore postulates that denial of hunger occurs in individuals who have a specific conflict about eating and who are also exposed to social pressure in this respect. It is concluded that in obese subjects the regulating mechanism of food intake is impaired and that the denial of hunger assists in the exclusion from awareness of any signals indicative of the subject's conflict in regard to eating.

A. Balfour Sclare

SCHIZOPHRENIA

445. **Periodic Schizophrenia.** (Sulla schizofrenia periodica)

A. Giannini and G. Del Carlo Giannini. *Rassegna di studi psichiatrici* [*Rass. Studi psichiat.*] **48**, 73–106, Jan.–Feb. [received Aug.], 1959. Bibliography.

Writing from the Psychiatric Clinic of the University of the Pisa the authors review the problem of certain periodic psychoses. In the great phase of clinical descriptive psychiatry periodicity was always an important criterion in the classification of mental diseases, and was a characteristic of one of the two great groups of endogenous psychoses described by Kraepelin, namely, manic-depressive psychosis. Periodic forms of the other main category, namely, schizophrenia, have also been described.

For some time now, however, psychiatrists have also recognized certain mental disorders which appear to occupy an intermediate position between manic-depressive psychosis and schizophrenia and which have some of the features of each. These schizo-affective disorders have been the subject of many reports in the literature, the chief of which are reviewed in this paper. The German school has recognized " atypical psychoses " which fall into two groups: (1) the " mixed psychoses ", in which dysthymic and schizophrenic symptoms alternate or are combined; and (2) " the degenerative psychoses " of Kleist, which represent variants of the manic-depressive psychosis to which are added confusional, paranoid, or hallucinatory elements. French authors on the other hand have tended to include under the blanket term " periodic psychoses " not only typical manic-depressive psychosis, but also all those atypical dysthymic forms containing elements of dissociation or confusion which run a periodic course.

The present authors give detailed histories of 7 patients, 4 women and 3 men, seen over the last 15 years in each of whom combined schizophrenic and manic-depressive symptoms occurred in periodic psychotic episodes, there being complete recovery in the intervals between episodes. These patients had in common an asthenic habitus, a basic schizoid personality, prompt recovery from the psychotic episodes after treatment with electric convulsion therapy, and absence of progressive mental deterioration. The authors state their reasons for regarding these psychoses as cyclothymic disorders with atypical symptomatology rather than as examples of schizophrenia running a periodic course.

J. B. Stanton

446. **Behavioral and EEG Changes Induced by Injection of Schizophrenic Urine Extract**

J. Wada and W. C. Gibson. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **81**, 747–764, June, 1959. 17 figs., 39 refs.

It has been suggested that the aromatic compounds detected chromatographically in the urine of schizophrenics differ not only quantitatively but also qualitatively from those in the urine of normal subjects. In the present study, reported from the University of British Columbia, Vancouver, extracts of the pooled urine from 10 normal subjects and from 20 male and female patients with acute schizophrenia of various types were injected into the cisterna magna of 9 normally friendly cats and 10 monkeys, and also into the lateral ventricles of 2 monkeys.

In the cats after the injection of extracts from normal subjects some reduction in activity and response was observed, but when caressed the animals responded by purring or playing, as formerly; a generalized seizure occurred in one case. However, after the injection of schizophrenic urinary extract none of the cats responded to caressing, most appeared frightened, double incontinence occurred in 3 instances, and 2 of the animals scratched their face and head with both forepaws intermittently for 20 minutes. A " rage state " lasting from 20 to 60 minutes developed in 5 of the cats, while the other 4 showed peculiar behaviour, 2 appearing to be searching for something only loud noises attracting their attention. When touched they appeared frightened and tried to escape; this behaviour persisted for about 20 to 30 minutes. Electroencephalographic (EEG) recordings showed high-voltage, sharp, slow, wave-and-spike discharges persisting for more than 5 hours. One cat ran around the cage foaming at the mouth some 7 hours after the injection, arching his back and looking scared, while another became rigid and stuporose about one hour after injection. In these animals the EEG

showed bursts of high-voltage, multiple, sharp, and slow waves, lagging a little behind the onset of the stuporose states.

The monkeys on the other hand showed marked docility after injection of both extracts, although they remained frightened if disturbed. Those receiving the schizophrenic urinary extract lost their fear. All were slightly ataxic, but appeared comfortable. The condition persisted for about 20 to 60 minutes, when the animals again became active, although the unwonted tameness lasted for more than 12 hours. One monkey, about 7 hours after the injection, repeatedly attempted to lick a flaming match. Generalized seizures occurred in 3 animals after both types of extract, these being followed by almost normal behaviour for about one hour. In 3 of the monkeys, between 2 and 4 hours after injection of the schizophrenic urinary extract, " blank " episodes occurred which lasted from a few seconds to 4 minutes during which they made no movement except for slow response to intense noxious stimulation. These episodes persisted for up to 12 hours after the injection, becoming progressively less frequent and less severe. The EEG was recorded in 2 monkeys. Before the injections a low-voltage, fast activity was set off by a slight noise or brusque movement of the experimenter. After the injections this response was less easily evoked during the docile state, and frequently failed to appear during the stuporose state, even when strong painful stimuli were applied. Although the eyes remained open, a typical light-sleep pattern in the EEG was seen during some stuporose episodes. On some occasions noxious stimuli produced faster EEG activity without the animal, however, becoming alert. *G. de M. Rudolf*

TREATMENT

447. **The Use of Intravenous Methylphenidate (Ritalin) in Psychiatric Interviewing**

A. B. KERENYI, E. K. KORANYI, and S. J. SARWER-FONER. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **80**, 963–967, June 15, 1959. 8 refs.

The authors, writing from the Jewish General Hospital, Montreal, describe the use of methylphenidate hydrochloride (" ritalin ") as an aid in psychiatric interviewing. The 40 patients taking part in the trial were selected for treatment on two main criteria: (1) that they had difficulty in talking freely about important and emotionally charged subjects; and (2) that they were free from severe mental illness. The drug was given in a dose of 20 to 40 mg. in 1 to 2 ml. of distilled water by rapid intravenous injection on 126 occasions, the patient first being told that the injection " would help him to relax ".

In most cases after about 3 minutes the patient began to respond more freely and, within the framework of the psychotherapeutic interview, was able to talk about early memories, sexual experiences, and transference feelings. In several cases there was a noticeable increase in motor activity, but severe agitation did not develop. A true emotional abreaction was obtained in only about one-third of the interviews, but it was noted that depressed patients tended to become more cheerful. Unwelcome side-effects were few and none were serious. After 28% of interviews the patient was over-talkative for 2 or 3 hours, while minor subjective complaints such as dryness of the mouth, dizziness, headache, flushing of the face, and shortness of breath each occurred in under 10% of cases and generally disappeared by the end of the interview. The authors conclude that methylphenidate hydrochloride is a safe stimulant which is likely to be of help in selected patients receiving psychotherapeutic treatment. *B. M. Davies*

448. **Treatment of Depressive States in Office Practice**

J. L. BELL, H. TAUBER, A. SANTY, and F. PULITO. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **20**, 263–267, June, 1959. 13 refs.

The authors describe the effects of " deprol " tablets (each containing a combination of 400 mg. of meprobamate and 1 mg. of benactyzine hydrochloride) in the treatment of 77 ambulatory depressed patients seen in private practice. They accept Alexander's definition of depression as " a state of sadness, with self-reproaches, psychomotor inhibitions, sleep disturbances, and impaired appetite."

The initial dose of deprol was 4 tablets a day, this being reduced as side-effects or improvement occurred. Treatment lasted one week to 3 months, with an average of 5 weeks. The outcome in each case was judged clinically and assessed according to defined criteria on a 4-point scale, the combined results being: recovered, 5; significantly improved, 33; some favourable effects, 19; and unimproved, 20. One of the 4 authors tended to award more pessimistic ratings than the other 3. The same rating scale was used for recording changes in individual symptoms, such as self-reproach, crying, and loss of interest in life, but no wide variations were found in the response of different symptoms. Of the 59 patients who had been previously treated with other drugs, 27 were rated as improved or recovered with deprol, whereas only 2 had improved with their previous treatment. Of the total of 77 patients, 53 were diagnosed as neurotic, 19 as psychotic, and 5 as " brain-damaged ". Of the neurotics, 34 were regarded as significantly improved or recovered compared with only 4 of the remainder.

The authors conclude that important benefits were produced in lessening cardinal symptoms of depression, especially among the neurotics. The action of the drug is prompt and relatively non-toxic. Side-effects were few and unimportant, 4 instances of drowsiness, 3 of dizziness, one of stomach upset, and one rash being noted. Doctor–patient rapport was thought to be better and psychotherapy facilitated by the use of deprol.

[The authors had no control group with which to compare their improvement ratings, although they state that deprol produced greater improvement than previous treatments. Unfortunately they do not mention or take into account the proportion of patients who improved sufficiently on other drugs not to require further treatment and were therefore excluded from the present inquiry.] *D. J. West*

Dermatology

449. **Prolonged Administration of Triamcinolone in Dermatologic Disorders: Therapeutic Efficacy and Side-effects**

N. B. KANOF, S. BLAU, R. FLEISCHMAJER, and B. MEISTER. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] 79, 631–634, June, 1959. 1 fig., 9 refs.

In this paper from New York University Post-Graduate Medical School the authors review the therapeutic efficacy of triamcinolone and the side-effects observed in the long-term treatment of a variety of dermatoses occurring in 75 patients (28 male and 47 female) ranging in age from 4 to 75 years. The dosage of the steroid varied from 8 to 32 mg. daily, the dose being gradually reduced to maintenance level whenever possible (average 8 mg. per day). Of the 75 patients, 58 received uninterrupted treatment for 3 to 16 months, 25 for 6 months or more, and 12 for over 10 months.

Marked improvement occurred in 35 out of 37 patients with atopic dermatitis, in 4 out of 5 cases of psoriasis, 11 cases of contact dermatitis cleared rapidly, and 2 cases of pemphigus erythematosus were well controlled, while in 2 patients with alopecia areata good regrowth of the hair was obtained. Treatment had to be discontinued in one case because of severe vertigo and nausea and in another because of abdominal pain associated with a peptic ulcer, which was probably present before treatment began. Other side-effects, not necessitating the withdrawal of treatment, included moon face in 8, acneiform eruptions in 8, abdominal discomfort and nausea in 7, hypertrichosis in 3, severe perspiration in 2, and one case each of glycosuria, headache, mental depression, and cellulitis. There were no significant changes in the blood pressure, and oedema was not observed, but 33 patients (13 of whom had previously received prednisolone) showed some loss of weight, while 14 gained weight.

[The mildness of the side-effects in this series after long-term administration of triamcinolone is encouraging, but nevertheless such effects did occur in more than 45% of the patients. The possible effects of withdrawal of the drug are not discussed.] *Benjamin Schwartz*

450. **The *p*H of the Skin Surface of Infants Aged One to Seven Days**

J. M. BEARE, E. A. CHEESEMAN, A. A. H. GAILEY, D. W. NEILL, and J. D. MERRETT. *British Journal of Dermatology* [*Brit. J. Derm.*] 71, 165–180, May, 1959.

At the Royal Maternity Hospital, Belfast, the *p*H of the skin surface at 34 body sites in 203 healthy infants (100 boys and 103 girls) aged 1 to 7 days was determined by means of a Marconi direct-reading *p*H indicator. The means for the two sexes were not significantly different. Important differences were consistently found, however, between corresponding flexor and extensor surfaces, the flexor surfaces having the higher mean *p*H. The dorsum of the hands, elbow points, and the extensor surfaces of the upper arms were the most acid areas and the groins, scalp, and forehead the most alkaline.

The authors could find no comparable data for children of this age in the literature, but the results obtained by other authors in older children suggest that changes in *p*H are associated with age, but not in a uniform manner at all sites. There was some evidence that children with seborrhoeic disease have a more alkaline skin surface reaction over the whole body than healthy children, and it is suggested that it might be possible to detect susceptible children long before this condition develops. For this reason information about *p*H levels in normal individuals at different ages would prove useful.

G. W. Csonka

451. **Studies on Melanoma. II. Sex and Survival in Human Melanoma**

L. P. WHITE. *New England Journal of Medicine* [*New Engl. J. Med.*] **260**, 789–797, April 16, 1959. Bibliography.

The observation that transplanted melanomata grow faster in male than in female mice prompted a follow-up study at Stanford University School of Medicine, San Francisco, of 439 patients with malignant melanoma.

The average 5-year survival rate was 34% in females and 23% in males. There were some small differences between the sexes in respect of certain factors making for a good prognosis (an excess of females in the age group 21 to 30, with consequent lower mean age at onset, and a higher incidence of melanoma of the arm and leg in females), but these accounted for only a small part of the total difference between the sexes. At all sites the prognosis deteriorated with age; for females the 5-year survival rate was 70% at age 21 to 30 and 21% at age 71 and over. There was also a marked increase in the incidence of face and scalp lesions with age. The author does not consider that his findings and the reported findings of others permit any firm conclusions to be drawn concerning the adverse effect of pregnancy or the menopause on prognosis. He states that the variation in behaviour of melanoma at times of hormonal disturbance, together with the better survival rate in females, suggests the possibility of some hormonal influence or control, but there is no direct evidence of this.

Bernard Lennox

452. **Local Antibiotics in Skin Infections**

I. C. LAMONT. *British Journal of Dermatology* [*Brit. J. Derm.*] 71, 201–210, June, 1959. 2 figs., 20 refs.

In this paper from Victoria Infirmary, Glasgow, the author discusses the bacteriology of impetigo and other infections of the skin and the relative efficacy of different antibiotics, with reference to an outbreak of impetigo in 1954 and of miscellaneous skin infections in 1957. The staphylococcus is still the cause of most skin infections; it was present in 78 out of 80 cases of impetigo, mostly of the bullous type. Pure streptococcal and pure

Gram-negative bacillary infections were uncommon, but the author points out that the possibility of these organisms being present in a mixed infection should not be forgotten when antibiotic therapy has to be started " blind ", as is generally the case.

Among out-patients resistance of staphylococci to penicillin and the tetracyclines is steadily increasing, but chloramphenicol and neomycin continue to be effective in action. Chloramphenicol, however, may produce severe epidermal sensitivity, and skin sensitivity to neomycin appears to be on the increase. Pure streptococcal infections are not a major problem and there is relatively little resistance to antibiotics, with the exception of neomycin. In mixed staphylococcal and streptococcal infections it is best to combine neomycin with either bacitracin or gramicidin. In Gram-negative bacillary infections chloramphenicol is more effective than penicillin, the tetracyclines, or neomycin. Skin sensitivity tests indicate that chloramphenicol is the antibiotic most likely to cure the majority of skin infections.

The author advocates the use of aqueous solutions of antibiotics—for example, 0·1% neomycin, 0·5% chloramphenicol, or 0·5% chlortetracycline—which should be applied by spraying or dabbing. He emphasizes, however, that the development of each new antibiotic is followed by a " steadily overtaking trail of resistance and even skin intolerance ". In his view the use of antibiotics in skin infections should be restricted as much as possible and non-antibiotic remedies used instead, particularly gentian violet, which is often effective in extremely weak solutions (1 in 30,000), scarcely staining the skin at all. *E. W. Prosser Thomas*

453. **Comparison of Topical Steroids**
P. INMAN. *British Journal of Dermatology* [*Brit. J. Derm.*] **71**, 211–213, June, 1959. 5 refs.

The author reports, from the Sunderland and West Hartlepool Skin Service, a comparative trial of an ointment containing 1% hydrocortisone acetate and an ointment containing 0·25% prednisolone in 25 cases of symmetrical eczema of the limbs, the hydrocortisone being applied to the right limbs and prednisolone to the left. The two preparations were equally effective, an occasional marked superiority of one or the other probably being due to a difference in the ointment base.
E. W. Prosser Thomas

454. **A Trial of Trimeprazine in Itching Dermatoses**
T. E. ANDERSON and D. CHALMERS. *British Journal of Dermatology* [*Brit. J. Derm.*] **71**, 214–218, June, 1959.

" Trimeprazine ", a recently developed phenothiazine derivative pharmacologically intermediate between promethazine (" phenergan ") and chlorpromazine (" largactil "), was tried in the treatment of itching dermatoses in 83 adults at Aberdeen Royal Infirmary and 53 children at the Royal Aberdeen Hospital for Sick Children. The adults received the drug in tablet form in a dosage of 10 mg. 4 times a day, and the results indicated that it was more effective than control tablets in relieving itching. Patients with atopic dermatitis and neurodermatitis responded particularly well. In an uncontrolled trial in patients with infantile eczema and juvenile atopic dermatitis trimeprazine was given in the form of a syrup in a dosage of 10·8 to 28·8 mg. daily according to age, weight, and the severity of itching. The majority of the patients appeared to benefit. There were no untoward side-effects. *E. W. Prosser Thomas*

455. **Bone Lesions of Urticaria Pigmentosa in Childhood**
M. H. LEES and C. E. STROUD. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 205–209, June [received Aug.], 1959. 6 figs., 28 refs.

The incidence of bone lesions in urticaria pigmentosa was studied in 32 patients at the Hospital for Sick Children, Great Ormond Street, London. Bone lesions were found in 4 of the patients and in a further 3 there were coincident abnormalities—coeliac disease, bacterial cholangiitis, and splenomegaly respectively. The case histories of all 7 patients are reported. Radiological examination revealed kyphosis in one patient whose spine, like that of another child, had the appearances of Scheuermann's disease, changes in the femora were seen in one patient and generalized osteoporosis in 2 patients. In one case examination of the bone marrow showed cells similar to those found in mast-cell leukaemia.
S. T. Anning

456. **Defective Epidermal Utilization and Storage of S^{35} in Psoriasis**
M. J. LIPNIK and S. H. LEVY. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **80**, 36–43, July, 1959. 3 figs., 13 refs.

The authors discuss previous reports that there is an increase in the sulphydryl content of the skin in psoriatic areas. They then describe their own findings in investigations with a radioactive isotope of sulphur (^{35}S), which was given by mouth to 9 adult patients with severe but not exfoliative psoriasis and 14 control subjects as part of the molecule of L-methionine, tests for the tracer substance being subsequently made on blood, urine, faeces, and normal and affected skin. The results are tabulated and illustrated graphically and show no significant difference between the patients and the controls in either the absorption or the excretion of the labelled sulphur compound. The ^{35}S content of psoriatic skin, however, was increased 2- to 6-fold over that of clear skin from psoriatic subjects and of the skin of the controls. Peak levels of ^{35}S were reached in 4 hours in normal skin, but the levels increased for up to 4 days in psoriatic skin, and at the end of one week the level of ^{35}S in psoriatic skin was still twice as high as the highest level found at any time in the controls. ^{35}S was also shown to be retained for a longer period in psoriatic clear skin than in the skin of control subjects.

The authors suggest that a defect in the kinetics of sulphur metabolism exists in psoriasis, with a deposition of sulphur-containing compounds in the skin. They note in this connexion that the successful standard treatments of psoriasis are those which are effective in oxidizing, mobilizing, or binding the SH groups in the skin. *Benjamin Schwartz*

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

457. **The Respiratory Distress Syndrome and Its Significance in Premature Infants**
W. A. BAUMAN. *Pediatrics* [*Pediatrics*] **24**, 194–204, Aug., 1959. 6 figs., 14 refs.

The significance of the respiratory distress syndrome in premature infants was studied in 201 patients admitted consecutively to the Premature Nursery of the Babies Hospital, New York, between December, 1956, and March, 1958. Each infant was examined every 6 hours for the first 72 hours of life for signs of respiratory distress, which were assessed according to the criteria of Silverman and Andersen, a score being given for the following physical signs: (1) see-saw movement of the chest, the sternum moving inwards as the abdomen moves out; (2) inspiratory indrawing of the intercostal spaces; (3) inspiratory retraction of the ziphoid cartilage; (4) descent of the chin on inspiration; and (5) an expiratory grunt. Each sign was scored 1 if present and 2 if marked; the maximum " retraction score " therefore was 10, and a score of 2 or more was considered to indicate the presence of the respiratory distress syndrome.

The incidence of significant signs varied inversely with the birth weight and diminished throughout the first 24 hours of life. Of the 201 infants, 37% had significant retraction in the first 6 hours of life and 19% at 24 hours. Of 43 infants who died in the first week of life, 33 had scores of 2 or more and 20 of these had hyaline membrane in the lungs; of the 10 infants who had no signs of respiratory distress, only one had a hyaline membrane. Approximately three-fifths of affected infants died in the first week of life compared with about one-tenth of those not affected.

The author concludes that the retraction score is a valuable prognostic aid, but since 40% of infants with clinical signs of respiratory distress survive without specific treatment any proposed therapeutic measures must be critically evaluated before they can be considered beneficial. *H. G. Farquhar*

458. **Hemoglobin Metabolism in the Premature Infant**
J. DANCIS, S. DANOFF, J. ZABRISKIE, and M. E. BALIS. *Journal of Pediatrics* [*J. Pediat.*] **54**, 748–755, June, 1959. 6 figs., 9 refs.

[Glycine containing] N^{15} [a non-radioactive isotope of nitrogen] was administered to 3 premature infants. The hemoglobin concentration and the N^{15} concentration in the hemoglobin were followed. The total circulating hemoglobin and the total N^{15} in hemoglobin were calculated using average figures for the blood volume. The following pattern was observed.

Phase 1, first 6 to 10 days, the N^{15} concentration rose rapidly as newly synthesized red blood cells containing N^{15} appeared in the circulation.

Phase 2, from 10 to 50 days, the N^{15} concentration rose more slowly while the total circulating N^{15} remained constant and the total circulating hemoglobin fell. In this period the rate of synthesis had slowed.

Phase 3, 50 to 80 days, the N^{15} concentration began to fall while the total circulating N^{15} remained constant and the total hemoglobin began to rise. This corresponds to a period of increased synthetic activity.

Phase 4, 80 to 130 days, the N^{15} concentration continued to fall and the total hemoglobin began to rise, but the total circulating N^{15} began to fall. During this period rapid synthesis of new cells continued and the tagged cells began to reach the end of their life span.

It is concluded that the anemia of prematurity results from a decreased rate of synthesis, the effects of which are exaggerated by the rapid growth of the infant and the increase in blood volume. The red blood cells have a normal life span. In one infant an iron-deficiency anemia occurred after the eightieth day of life. The changes in N^{15} concentration indicated a slowing in rate of synthesis. In another infant there was an abrupt drop in total circulating N^{15} about the sixtieth day of life, suggesting a hemolytic crisis. This occurred in the absence of clinical signs and would not have been detected by conventional methods of study.—[Authors' summary.]

459. **Hyperbilirubinemia in Premature Infants: Follow-up Study**
C. A. KOCH, D. V. JONES, M. S. DINE, and E. A. WAGNER. *Journal of Pediatrics* [*J. Pediat.*] **55**, 23–29, July, 1959. 17 refs.

At Cincinnati General Hospital serial estimations of the serum bilirubin level were carried out in 1953 by one of the authors (Dine) in 100 consecutive newborn premature infants who neither suffered from sepsis nor showed any evidence of isoimmunization. The infants were observed carefully for the first few weeks of life and then re-examined between 2 and 3 years later. Many of these infants had received up to 10 mg. of vitamin K daily, a not unusual procedure in 1953. Of the 8 infants dying in the neonatal period, 2 were found at necropsy to have kernicterus; in both these cases the serum bilirubin level was above 20 mg. per 100 ml., whereas in the other 6 cases the bilirubin value remained below this level. In the present follow-up study 49 survivors of the original 100 were re-examined in 1955 and 1956. Neuromuscular abnormalities attributable to kernicterus were found in 5 patients, 4 being mentally retarded and either spastic or athetoid, while the remaining child was deaf and walked with a wide-based gait. In 31 of the 49 infants the maximum serum bilirubin level at birth was below 20 mg. per 100 ml. and all these infants were normal, but of 14 in whom this level had been between 20 and 30 mg. per 100 ml., 2 were affected, while of the 4 infants with a serum bilirubin level above 30 mg. per 100 ml., 3

were affected. There was no clear relationship between the later development of kernicterus and the vigour of the infant at birth or the birth weight.

In discussion the authors stress that the 5 abnormal infants did not differ noticeably from the normal children in the early weeks of life; thus none had convulsions or hyperirritability, and the 2 with the highest serum bilirubin levels were vigorous and active and took their feeds well. It is suggested that careful observation over several years is therefore necessary to detect the true incidence of brain damage. They conclude that a high serum bilirubin level is the most important aetiological factor in kernicterus and advocate that when this level rises above 20 mg. per 100 ml. exchange blood transfusion should be given. *F. P. Hudson*

460. **Ammonia Metabolism in Normal Newborn Infants and Those with Idiopathic Hyperbilirubinemia**
J. J. McGovern, W. V. McDermott, M. N. McGovern, M. Russell, E. McGrath, and A. Holtz. *Pediatrics* [*Pediatrics*] **23**, 1160–1167, June, 1959. 5 figs., 20 refs.

It has been suggested that the high concentration of ammonia in the blood of newborn infants and in stored blood may have some bearing on the development of kernicterus in infants given exchange transfusion. The authors have therefore determined the concentrations of ammonia nitrogen in the blood withdrawn at different sites in normal newborn infants and their mothers and in infants with high bilirubin levels born at St. Margaret's Hospital, Boston. The mean blood levels of ammonia in 53 normal newborn infants during the first 5 days of life were 101 μg. per 100 ml. in the femoral vein, 103 μg. per 100 ml. in the femoral artery, 148 μg. per 100 ml. in the umbilical vein near the portal vein, compared with 55 μg. per 100 ml. in the antecubital vein of the mother. By the 10th day of life, however, the levels in the infants had fallen to the adult level. The ammonia levels in jaundiced infants varied with the cause of the jaundice; for example, in 9 infants with erythroblastosis foetalis the blood ammonia level averaged 97 μg. per 100 ml. in the first 5 days of life, but in 26 infants with idiopathic hyperbilirubinaemia the average concentration for the same period was 133 μg. per 100 ml. There was no significant correlation between the degree of jaundice and the blood ammonia concentration. The possible causes of the high ammonia levels in blood taken from the umbilical vein near the portal vein in the newborn baby are discussed. *R. M. Todd*

461. **Heme Pigment and Bilirubin Rebound following Exchange Transfusions in Infants with Erythroblastosis Fetalis**
G. K. Summer and J. P. Goulson. *Journal of Pediatrics* [*J. Pediat.*] **55**, 30–34, July, 1959. 4 figs., 8 refs.

High serum levels of bilirubin are clearly associated with the development of kernicterus in infants, and bilirubin has been shown experimentally to inhibit oxidative phosphorylation in isolated rat brain cells. Mesobilirubin and hematin have similar toxic actions and the authors, writing from the University of North Carolina, Chapel Hill, suggest that the deleterious effects of hyperbilirubinaemia may be the result of competition between bilirubin and heme pigments in the respiratory enzyme activity of the brain.

They have therefore determined, in 3 infants suffering from erythroblastosis foetalis who received 2, 3, and 4 exchange transfusions respectively, the levels of bilirubin and heme pigment in the serum before and after treatment. Spectrophotometric absorption patterns of bilirubin and heme pigment were determined with a Beckman spectrophotometer and the serum bilirubin concentration measured by the van den Bergh diazo reaction. The results, presented in three charts, show that there was a rapid and variable rise in the serum content of bilirubin and heme pigments in each case following exchange transfusion. It is suggested that these substances, which are both bound to protein, come from an extravascular reservoir and are drawn to protein-binding sites in the transfused plasma. However, the mechanism by which bilirubin and heme pigments inhibit respiration of brain and other cells remains to be elucidated.
F. P. Hudson

462. **Some Observations on Listeriosis in the Newborn.** (Beobachtungen bei Listeriose der Neugeborenen)
F. W. Wedemeyer and H. P. R. Seeliger. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **160**, 25–37, 1959. 1 fig., 10 refs.

The authors describe 5 cases of generalized listeriosis in newborn infants treated at the St. Bernwald Hospital, Hildesheim, during 1956–8. They give a fully documented account of the clinical findings and maternal and infant serology in all the cases and of the macro- and microscopic post-mortem findings in 2 of them.

The clinical picture was exceedingly variable and no consistent cardinal signs were found. Four of the cases presented at birth or within a few hours of birth, and one after 24 hours of apparent good health. Three of the infants had a fine haemorrhagic papular rash. Three were moribund, with generalized cyanosis, central respiratory depression, hypotonia, and areflexia, one was in white asphyxia, and one had acute respiratory distress. Radiography of the chest in this last case and one other showed miliary opacities. Blood counts showed no consistent change apart from slight monocytosis in 2 cases. Fever was present towards the end of the first day of illness in all cases. Two patients were jaundiced. In one case the cerebrospinal fluid was blood-stained and in another it was xanthochromic. Three of the mothers had had fever during childbirth, one had meconium-stained liquor, and one had proteinuria. One had a past history of one abortion and one child dying in the neonatal period.

Bacteriological and serological methods were of little use in early diagnosis. The view that *Listeria monocytogenes* is always demonstrable in Gram-stained preparations of the meconium in cases of this type was not borne out. Emphasis is placed on the value of Gray's method of culture for *Listeria* (preculture of meconium at 4° C. for up to 6 weeks). In one case a positive culture was obtained only after 5 weeks' preculture and the bacteriological confirmation would have been missed by standard methods. In another case, however, the

culture was positive in less than 24 hours. An increased antibody titre was found in 4 of the infants, and in all these cases the maternal titre was also raised. The maternal titre is not increased in all proven infections, nor is the presence of a high titre sufficient alone for diagnosis, though titres in excess of 1:320 are usually significant. Both agglutination and complement-fixation methods were used, but their results did not run parallel; their combined use is recommended as a routine. The titre fell in one mother after treatment with tetracycline.

Treatment in 3 of the 4 fatal cases was with penicillin and sulphonamides and in the other with oxytetracycline. The only surviving infant received penicillin, streptomycin, and sulphonamide for the first 4 days without improvement and was then given chloramphenicol in a dosage of 35 mg. per kg. body weight per day. There was complete recovery.

The authors conclude that listeriosis will be diagnosed far more commonly when all available diagnostic techniques are fully used. Treatment should be begun on suspicion only, as there is no typical clinical picture and no conclusive early diagnostic test is available. The diagnosis must usually be confirmed retrospectively by meconium culture and maternal and infant serology.

Julian Tudor-Hart

463. **The Effect of Maternal Narcotic Addiction on the Newborn Infant: Review of Literature and Report of 22 Cases**

R. W. COBRINIK, R. T. HOOD, and E. CHUSID. *Pediatrics* [*Pediatrics*] **24**, 288–304, Aug., 1959. 42 refs.

CLINICAL PAEDIATRICS

464. **Congenital Muscular Torticollis in Infancy. Some Observations Regarding Treatment**

M. B. COVENTRY and L. E. HARRIS. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **41A**, 815–822, July, 1959. 3 figs., 7 refs.

Of 7,835 infants born in Rochester, Minnesota, between January, 1944, and December, 1954, 35 had sternomastoid tumours with torticollis, 30 of these being examined at the Mayo Clinic one year or more after birth and the remainder followed up elsewhere. In about half the patients the tumour was first noticed by the mother. The authors consider that tumours are present at some stage in all cases of torticollis. In most cases the tumour appeared at 3½ weeks and disappeared at 3½ months. Facial asymmetry became evident after torticollis had developed and disappeared after the torticollis had been corrected. Physiotherapy alone was given to 24 patients, with excellent results. Operation was necessary in 5 cases, the tumour, when present, being excised at the time of division of the sternoclavicular attachment. There were 2 operative failures, these being attributed to the fact that the neck was not fixed in the over-corrected position at the time of operation. The remaining 6 patients in the series were not treated, but all did well.

The cause of the condition is not known, but the authors do not consider that it is due to muscle tearing or haemorrhage at birth. In vertex deliveries the left side was affected twice as often as the right, and in breech presentations the right twice as often as the left. Differential growth is not considered to be a cause of torticollis.

Charles Nicholas

465. **Results of Treatment of Congenital Dislocation of the Hip**

I. V. PONSETI and E. R. FRIGERIO. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **41A**, 823–846, July, 1959. 17 figs., 14 refs.

The anatomical results of treatment, from 1942 to 1950, of patients under 4 years old with congenital dislocation of the hip and those with preluxation treated from 1942 to 1954 have been reviewed. Thirty-two patients with 39 hip preluxations with a minimal follow-up of 4 years, 6 with 7 subluxations, and 58 patients with 74 hip dislocations and 4 subluxations with a minimal follow-up of 8 years were included in the study. The dislocations were reduced with the child under general anaesthesia; only 3 open reductions were done when closed reduction failed. Rotation osteotomy was done on 13 patients.

Good anatomical results were obtained in all cases of preluxation and subluxation (Groups I and II). Good anatomical results were also obtained in 52 of the dislocated hips; a dysplastic hip resulted in 11 instances. Thus, the femoral head was in a correct position in the acetabulum in 63 of the 74 dislocated hips. Moderate subluxation developed in 5 hips and severe subluxation in 6. No redislocation occurred. Closed reduction followed by carefully supervised treatment offers satisfactory results in the majority of congenital dislocations of the hip if a child is seen before he is 4 years of age.

The importance of early treatment is apparent when the cases are divided into three groups. Good anatomical results were obtained in (*a*) all patients initially treated before the age of one year; (*b*) 78% of patients who were 1 to 2 years of age; and (*c*) only 57% of those who were 2 to 4 years of age. Early treatment offers the only possibility of obtaining good results almost regularly. The orthopaedic surgeon must collaborate with the pediatrician to discover all cases of congenital dislocation of the hip in early infancy. Ortolani's snapping sign is the only unequivocal sign of early dislocation.—[Authors' summary.]

466. **Association of Type 2 Hemadsorption (Para-Influenza 1) Virus and Asian Influenza A Virus with Infectious Croup**

A. J. VARGOSKO, R. M. CHANOCK, R. J. HUEBNER, A. H. LUCKEY, HYUN WHA KIM, C. CUMMING, and R. H. PARROTT. *New England Journal of Medicine* [*New Engl. J. Med.*] **261**, 1–9, July 2, 1959. 11 refs.

The possible viral aetiology of infectious croup was studied in 47 cases admitted to the Children's Hospital of the District of Columbia, Washington, between October, 1957, and September, 1958, these 47 cases representing 5·7% of all cases of respiratory illness in

children admitted during the 12-month period. Viruses were isolated from 16 cases. Paired specimens of serum were available in 38 cases, and 27 of these showed rises in antibody titres for different viruses. By one or both of these methods a viral infection could be specifically identified in 30 of the 47 cases.

The virus most frequently identified as the cause of infection was haemadsorption virus Type 2, one of the group of myxoviruses, which was associated with illness in 17 cases. Influenza-A (Asian) virus was the next most frequent cause (this study was carried out during an epidemic) and accounted for 9 cases. Other viruses identified were haemadsorption virus Type 1 and croup associated virus.

During the same period a much larger group of infants and children without respiratory illness were studied in the same manner. Infections with the same viruses occurred in less than 1% of the cases and positive titres were obtained in less than 10%. *John Fry*

467. **Bronchiectasis in Children: Its Multiple Clinical and Pathological Aspects**
H. WILLIAMS and R. N. O'REILLY. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 192–201, June [received Aug.], 1959. 8 figs., 25 refs.

The authors have reviewed 241 cases of bronchiectasis in childhood which were studied at the Royal Children's Hospital, Melbourne, from the beginning of the disease for 4 to 10 years, subdividing them into the following groups: (1) subacute pyogenic pulmonary collapse (37); (2) non-specific infective bronchiolitis and/or interstitial pneumonia (57); (3) fibrocystic disease of the pancreas (56); (4) primary pulmonary tuberculosis (53); (5) congenital malformations of the bronchial tree (16); and (6) miscellaneous lung infections (22). Only the first two groups are considered in detail in this paper.

The category of subacute pyogenic pulmonary collapse contains cases with onset between ages 2 and 6 years, usually following acute infection, the cough drying up after a course of one or 2 years. The main differentiating feature is the presence of collapse of the lobe at first. The group therefore includes a number of reversible cases, and complete or nearly complete resolution occurred in 30 out of the authors' 37 cases. The condition was usually unilateral and the responsible organisms were identified in about half the cases. There was no family history. Treatment was by chemotherapy and postural drainage.

Non-specific bronchiolitis and/or interstitial pneumonia is considered to be a separate condition in which some destructive mural bronchitis or other permanent change is postulated. In the authors' cases which fell within this group the onset was usually before the age of 2 years, and in three-quarters of them it was insidious. Upper respiratory infection was usually present and treatment by chemotherapy was less effective, although in most cases the symptoms became less severe between the ages of 10 and 14 years.

The condition was often bilateral and was never reversible, and no specific pathogens were recognized. The family history was generally positive. This group was further divided into those with generalized (11), localized and less severe (19), and progressive lesions (27). Even here most patients in the first two categories improved. In 7 of the progressive cases lobectomy was performed to remove all bronchiectatic areas, but all 7 patients developed bronchiectasis in another lobe. The authors recommend deferment of surgery until the second decade at the earliest because of the risk of spread and because of the general tendency towards improvement in these cases.

[The authors have made a valiant and worth-while effort to clarify the problem of bronchiectasis. Nevertheless, two comments must be made. First, the authors say that no special measures were taken to grow *Haemophilus influenzae* from the sputum, and in these circumstances it is difficult to attach much value to their observations on bacteriology. And second, many students of this subject omit from consideration cases of reversible bronchiectasis associated with collapse, and it may only confuse the problem to try to identify a group which, while it is mainly composed of reversible cases, has in it a small proportion of persistent true bronchiectatics. The study shows once more the generally favourable course of this disease under modern conditions. The relatively high incidence of progressive cases observed by the authors is unusual, and it would be valuable to have further information about these patients.]
A. White Franklin

468. **Congenital Choanal Atresia**
R. G. MACLEAN and W. HAMMACK. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **70**, 137–138, July, 1959. 1 fig., 15 refs.

More than 500 cases of congenital choanal atresia have been reported in the literature, but only 10 families have been recorded in which this anomaly was found in 2 or more members. In the family reported here the father had a complete right bony atresia which was cured by operation at 17 years of age, one child had a bilateral occlusion which was treated successfully by transpalatal approach at 6 weeks old, and a second child has a right unilateral occlusion which is awaiting operation. It is noteworthy that some members of the maternal grandmother's family died in the neonatal period, though in none had choanal atresia been recognized.
F. W. Watkyn-Thomas

469. **Surgery for Bilateral Bony Atresia of the Posterior Nares in the Newborn**
H. H. BEINFIELD. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **70**, 1–7, July, 1959. 8 figs., 5 refs.

It is recognized that bilateral atresia of the bony nares causes suffocation in the newborn as the infant will not normally open its mouth to breathe. The author describes 3 cases in which a life-saving airway was established by a simple method of perforating the occluding structure and intubating with a tube drawn up through the nasopharynx. As " first-aid " treatment an adequate supply of air can be obtained by keeping an infant-size airway in the mouth until the operation, which should be performed within the first 24 hours of

life, has been completed. The longer operation is delayed, the greater is the danger. All 3 patients survived. *F. W. Watkyn-Thomas*

470. **Muscle Tone and Posture in Infancy**
T. T. S. INGRAM. *Cerebral Palsy Bulletin* [*Cerebral Palsy Bull.*] No. 5, 6–15, 1959. 10 figs., 13 refs.

The author of this paper from the University of Edinburgh first describes the orderly sequence of changes in posture and its control and in muscle tone which occur during maturation in the normal infant. He then compares these with the findings in children suffering from bilateral cerebral palsy.

The primitive reflexes characteristic of infancy disappear in a consistent and predictable order as the higher centres come into play. They thus form a guide to the level of motor maturation. The normal newborn infant lies on one side with head, trunk, and limbs semiflexed and tends to return to this position after active or passive movement. A sudden movement or loud noise causes a momentary involuntary extension of the neck, trunk, and limbs—the Moro or "startle" reflex—after which the posture of semiflexion is gradually resumed. The response to the tonic neck reflex is greater in the flexor muscles than in the extensors during this period, which may be described as the "first flexor stage". At about the time when the child can hold up his head momentarily the "first extensor stage" begins. He does not return to the extreme semiflexed position after the Moro response, and extensor postures tend to persist after any movement. The tone in the extensor muscles increases and that in flexors decreases. The tonic neck reflex movements are more marked in the extensors than in the flexors, but this reflex now becomes difficult to elicit. There is marked hypertonus in the anti-gravity muscles, and when the child is placed erect, putting pressure on the soles of his feet, the increased tone in trunk and limb extensors will hold him upright with the minimum of support. This stage lasts only about 6 to 8 weeks, when the child is between 4 and 6 months old. The flexors now increase in tone and the baby is able to flex his trunk voluntarily and sit without support. When held upside down by the feet he flexes the neck, back, and limbs instead of extending them as he did previously. This "second flexor stage" is less well defined than the first, chiefly because of the greater amount of highly coordinated motor activity. Towards the end of the first year it gradually merges into the "second extensor stage", during which the baby starts to crawl and attempts to climb up objects. If held upside down he now extends his body and neck and looks at the floor, while postural changes produce less marked muscle responses. Next he stands, first with and then without support, and finally walks.

In cerebral palsy there is a retardation of neuromuscular maturation or a failure of the higher coordinating centres to develop. Development may cease at any point, and the most severely affected microcephalics never pass beyond the first flexor stage. In diplegia there is a retarded but orderly progression through the normal stages, but each stage may take months instead of weeks and movements tend to be gross and uninhibited. In the first extensor stage sudden transient attacks, in which the whole body is thrown into hyperextension with the limbs adducted, occur when the head is allowed to fall back, and this is often the first abnormality noticed by the parents. Sitting unsupported is impossible at this stage as the child cannot voluntarily flex his trunk, while he can "stand" only in the sense of the reflex extension found in the normal baby of 4 to 6 months. The limbs are rigid, resisting both flexion and extension. In some cases neuromuscular maturation ceases at this stage, but in most there is a gradual increase of flexor tonus and a decrease of extensor hypertonus, with spasticity of the limbs, only extension being resisted. However, the anti-gravity extensor responses may be marked and the "extensor thrust" whenever the child is placed erect can be very troublesome. Later these extensor responses diminish and flexor reflexes become exaggerated, flexion contractures developing in spite of treatment. Children with the athetoid, choreo-athetoid, or dyskinetic type of cerebral palsy progress similarly, but the characteristic involuntary movements appear at about the time head control is gained. These are due to transient extensor hypertonus. They vanish progressively in a cephalocaudal direction as the child matures.

Janet Q. Ballantine

471. **The Neurological Examination of Infants.** (Неврологическое исследование ребенка в возрасте до года)
S. KUPERNIK. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **59**, 808–815, No. 7, 1959. 14 figs.

The usual methods of neurological examination are not suitable for use in children under one year of age, since they are based on the normal development of the central nervous system (C.N.S.) at a later stage and moreover at this age the young infant cannot cooperate to assist in the examination. It should be remembered that signs which at an early age are normal may be pathological in a child a few months older, since the C.N.S. is undergoing rapid evolution.

The examination of the infant therefore is based on the primitive automatisms which govern the normal C.N.S. at that age. Earlier workers have emphasized the value of the Moro reflex, which is best elicited by raising the child by the legs without moving the head from the pillow; a response consisting in extension and abduction of the arms followed by their return to the mid-line (the so-called "embrace reflex") is the normal reaction to this movement in the first 8 weeks of life, but its persistence after the 6th month is evidence of severe damage to the C.N.S. The same is true of the "extension reflex", in which the child is held by the examiner under the arms and raised to a standing position with the feet pressing on the floor or bed; this should produce a progressive extension of the body, first of the lower extremities, then of the trunk, and lastly of the neck. So also with the "stepping reflex", in which the child is again supported in the standing position with the body leaning slightly forward, whereupon it makes automatic step-

ping movements, unassociated with any ability to balance itself or with any movements of the upper limbs. Likewise, the " prone crawling reflex " and the " grasping reflex " should disappear between the 4th and 6th months, soon to be replaced by purposeful movements in which all the limbs take a part.

Further examination of the infant should include a test for muscle tonus, especially in the muscles of the wrist, forearm, and neck. Passive turning of the head from side to side and of the wrist on the forearm is most valuable in eliciting evidence of diminished or excessive tonus. Next, the posture of the child as a whole should be carefully studied. A child under the age of 4 months cannot maintain itself in the sitting position, but should be able to support its head when lifted into that position; at 6 months it can support itself with the help of its arms, and at 8 months should be able to sit unsupported. At the latter age, if stood upright, it protrudes the buttocks and cannot stand unsupported, because the normal spinal curves have not yet developed, these appearing about the end of the first year. Raising the child by the arms with its feet braced against a block will reveal its power to support the head, which it should be able to do at the 6th month. Of these postural-locomotor reflexes, one of the most valuable is the " diving reflex ". This is elicited by raising the child horizontally in the prone position, and then quickly bringing it down towards the bed with the head tipped downwards and forwards, as in diving; to this manœuvre an infant of 2 months will respond by flexing the elbows, but between the 8th and 10th months the normal child will extend its arms with hands forwards, as though to protect its head. This reflex precedes the ability to walk, and its absence at 8 to 10 months is significant of cerebral damage or defect. Lastly the response of the eyes to sideward and rotatory movements of the head or to light, the presence of nystagmus, the response to sounds, and the power to imitate the movements of adults (for example, smiling) are all phenomena which indicate the state and development of the sensory system and of the power of the child to respond to its environment. *L. Firman-Edwards*

472. **Post-encephalitic Behavior Disorder—a Forgotten Entity: a Report of 100 Cases**

S. LEVY. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **115**, 1062–1067, June, 1959. 13 refs.

The author emphasizes the importance of an accurate differential diagnosis between ordinary juvenile " behaviour disorders " and those due to organic brain damage following encephalitis. He claims that the diagnosis can be easily made provided the possibility of a post-encephalitic syndrome is borne in mind, when the following outstanding signs are usually present: (1) hyperkinesis with either choreiform or tic-like movements; (2) inability to maintain quiet attitudes; (3) clumsiness of movement; (4) explosive motor release of all voluntarily inhibited activities. The aetiology usually includes a history of brain damage by high forceps delivery, or of a severe infectious disease in infancy, or frequent attacks of hyperthermia without apparent cause. The parents' description of the disorder shows that it is expressed almost entirely in the volitional sphere. The child is overactive, restless, shows a short attention span, is unpredictable, destructive, and usually incapable of showing remorse. School reports confirm the child's " inability to apply himself ". Physical and neurological examination are usually negative, but recently the photo-leptazol threshold test has shown significant differences between hyperkinetic and non-hyperkinetic children. The I.Q. is usually normal or higher and psychological testing does not contribute to the aetiology. The child is intolerant of frustration and seems unable to delay gratification of his demands.

Some 20 years ago amphetamine sulphate was introduced for the treatment of this disorder and the results in the series of 100 such patients here presented again show the effectiveness of the drug. It was given in doses of 10 to 40 mg. daily either in a single dose in the morning or with a second " booster " dose at lunch time half the strength of the first. In some cases the beneficial effect was delayed for 2 or 3 weeks, but once apparent it was spectacular. Restlessness and irritability decreased and the child's concentration span increased markedly. The patients became less " driven " in their behaviour and their parents and teachers responded much more favourably. Side-effects were few. In one case the child was either very sensitive to the drug or the diagnosis was at fault, as he became more disturbed over a long period, while in another case the patient developed a delayed dermatitis, but these were the only two in which the drug had to be discontinued. The author recalls that the drug must be given over a prolonged period, and recommends that parents should be warned that during the first 2 weeks of treatment the child's behaviour reactions may become exaggerated; however, provided that these reactions do not persist for more than 3 weeks this is a good prognostic sign. In view of the efficacy of amphetamine sulphate in the treatment of this disturbing and chronic illness it is particularly important that behaviour disorder when due to encephalitis should not be treated as a psychogenic illness. *M. R. Medhurst*

473. **The Diagnosis of Mental Retardation in Infancy: a Follow-up Study**

R. S. ILLINGWORTH and L. B. BIRCH. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 269–273, June [received Aug.], 1959. 14 refs.

In this paper from the University of Sheffield a follow-up study is reported of a series of 101 children who had shown evidence of mental retardation before the age of 2 years, the series being unselected except that cases of mongolism, cretinism, hydrocephalus, and anencephaly were excluded. The original diagnosis was made on the basis of the results of simple tests from the Gesell schedules, attention also being paid to the developmental history. The children were re-examined when aged 5 to 10 years, the usual test employed being that of Terman and Merrill. It was found that 59 of the children had an I.Q. of 50 or below, 24 an I.Q. of 50 to 75, 13 one of 76 to 94, and 5 an I.Q. of 100 or above. While only 4 children, including 3 with cerebral palsy, fared worse than expected, 16 fared better. *G. de M. Rudolf*

Medical Genetics

474. **Medical Genetics—1958.** [Review Article]
V. A. McKusick. *Journal of Chronic Diseases* [*J. chron. Dis.*] **10**, 256–363, Oct., 1959. Bibliography.

475. **Genetic Factors in Predisposition to Pernicious Anemia**
P. A. McIntyre, R. Hahn, C. L. Conley, and B. Glass. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **104**, 309–342, June, 1959. 8 figs., bibliography.

The criterion of predisposition to pernicious anaemia used in this study from the Johns Hopkins Hospital and University was impairment of absorption of vitamin B_{12} (cyanocobalamin). The authors examined 106 relatives of 34 patients with pernicious anaemia in whom the diagnosis was well documented. The mean age of the relatives was 36·23 years; 52 were male and 54 female; 4 were parents, 23 sibs, 55 children, and 24 less closely related. A control group of 97 normal subjects, 62 male and 35 female with a mean age of 30·35 years, was also studied. The controls were all white, whereas 17 of the relatives were negroes. Each subject was given 0·5 μg. of vitamin B_{12} labelled with radioactive cobalt (^{60}Co) by mouth and 1,000 μg. of unlabelled vitamin B_{12} intramuscularly one hour later; urine was collected for 25½ hours after the oral dose. The results were expressed as the percentage of administered radioactivity appearing in the urine, and reasons are given for believing that this was an adequate measure of absorption.

The findings are listed individually and also presented graphically. The control subjects excreted from 8·4 to 36% of the dose, the value in most cases being 15 to 30%; distribution showed a single mode in the range 19·1 to 22%. The relatives excreted 4·2 to 37·5%, the distribution of values showing one mode at 16·1 to 19% and another at 10·1 to 13%; there were few high values.

The difference between the groups was not attributable to sex or racial difference. No relation was found in the control group between excretion of vitamin B_{12} and age, but among the relatives excretion diminished markedly with age; yet age alone did not account for the difference between the groups. Within the families of patients with pernicious anaemia low values were found both in the same and in successive generations. One or both parents of 32 subjects from both groups whose excretion was abnormally low were tested, and in 30 cases a parent also showed low excretion. The frequency of low excretion (less than 15%) among the children of patients with pernicious anaemia, when corrected for their youth, was 38·2%, which is not significantly lower than that among the patients' sibs, which was 48%. Hence low excretion is unlikely to be due to a recessive gene whose frequency in the general population is such as would produce the proportion of low values (10%) found in the control group; and it could not be due to a gene which caused low excretion in heterozygotes and pernicious anaemia in homozygotes. The authors prefer the hypothesis of an autosomal gene causing low absorption of vitamin B_{12} in the heterozygote, who may then develop pernicious anaemia; they consider that the decrease in absorption with increasing age may be separately determined. *G. C. R. Morris*

476. **Medullary Gonadal Dysgenesis (Chromatin-positive Klinefelter's Syndrome): a Genetically Determined Condition with Eunuchoid Measurements but Early Epiphyseal Closure**
J. S. S. Stewart. *Lancet* [*Lancet*] **1**, 1176–1178, June 6, 1959. 3 figs., 11 refs.

This report from the Royal Infirmary, Glasgow, describes the findings in one adult and 4 adolescent patients with Klinefelter's syndrome. One of these, a man of 27, attended hospital because of sterility, another, a boy of 14, because of gynaecomastia, and a third, a lad of 19, because of nocturnal enuresis; the 2 remaining boys, aged 15 and 16 respectively, were found in a survey of 182 boys of these ages at schools for mentally handicapped children. All 5 patients had small testes and one had marked and 2 slight gynaecomastia; in all cases buccal smears were chromatin-positive and testicular biopsy confirmed the diagnosis. Culture of testicular material from the man allowed his chromosomes to be counted: there were 47 pairs, and the sex chromosomes appeared to be XXY.

Measurements of height, arm span, sole to pubis, and crown to pubis are given, with true and bone ages. Arm span exceeded height by 4 inches (10 cm.) in the man, and by 1⅜ and 2¾ inches (3·5 and 7 cm.) in boys of 15 and 16. Sole to pubis length was greater than crown to pubis length in all, by 1½ inches (3·8 cm.) in the boy of 15, by 3½ to 4¼ inches (8·9 to 10·8 cm.) in the others. The boys' bone ages were 1 to 5 years more than their chronological ages. Their daily urinary output of follicle-stimulating hormone was high (40 to 80 mouse units in 2 and >80 units in 2) and that of 17-ketosteroids normal.

The author contends that the chromosomal evidence supports the genetic aetiology of the condition. He points out that the usual eunuchoid body measurements, found also in these cases, can hardly be due to late closure of epiphyses, since closure was early in these boys; he suggests there may be increased activity of growth hormone. The discovery that the sex chromosomes in Klinefelter's syndrome are XXY, whereas in Turner's syndrome they are XO, suggests that two X chromosomes are necessary for the development of the cortex and a Y chromosome for the development of the medulla of the gonad. A revision of nomenclature is therefore proposed, Klinefelter's syndrome being an example of medullary gonadal dysgenesis and Turner's syndrome one of cortical gonadal dysgenesis. *G. C. R. Morris*

Public Health and Industrial Medicine

477. **Tobacco Consumption and Mortality from Cancer and Other Diseases**

H. F. DORN. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **74**, 581–593, July, 1959. 7 figs.

In January, 1954, a questionary was sent to all policy holders of United States Government life insurance, all of whom had served in the armed forces between 1917 and 1940 and the majority of whom were veterans of the first world war, asking for information about their tobacco-smoking habits. Replies were received from 198,926 persons (68%), giving a total of "478,952 person-years exposure, of which 89,774 were contributed by persons who had never smoked and 389,178 by persons who had smoked tobacco in some form during their lifetime". These policy holders were classified according to their past and current smoking habits into carefully defined categories and the mortality experienced by the group during the next 2½ years was studied in relation to this classification. The cause of death given on the death certificate presented in support of a claim was verified, as well as additional details obtained, by reference to the certifying physician.

In presenting the results the author compares the number of deaths observed in each smoking-history category with the number which would have been expected if the smokers had experienced the same age-specific death rates as the non-smokers, this comparison being expressed as a mortality ratio (observed:expected). However, a table is also included which shows the deaths from all causes combined per 1,000 per year in 8 age groups for the non-smokers and the 12 categories of smokers. The greatest divergence from the age-specific mortality of non-smokers occurred among persons who had regularly smoked only cigarettes. In this category the death rates per 1,000 per year were as follows, the rates for non-smokers being given in brackets: at age 30–39, 1·2 (0·7); at age 40–49, 3·4 (2·9); then in successive 5-year age groups, 10·4 (6·6), 15·3 (9·0), 22·9 (14·8), 33·4 (21·6), and 49·8 (35·8); and at ages 75 and over, 84·7 (70·0). The rates for persons who had regularly smoked cigars, pipes, or both were slightly higher than for non-smokers, while those for smokers of cigarettes in addition to cigars or pipes were intermediate between these and the rates for smokers of cigarettes only. Regular smokers of cigarettes only who had given up smoking before 1954 ("ex-smokers") had a lower mortality than those who continued to smoke; thus the mortality ratio for ex-smokers was 1·39 compared with 1·65 for those who were still smoking. For ex-smokers of cigars, pipes, and both the mortality ratios were higher (1·44, 1·25, and 1·21 respectively) than for those who continued these habits (0·94, 1·05, and 1·04 respectively). The latter ratios do not indicate any material difference from the mortality of non-smokers, and a possible explanation of the unexpected finding of a higher mortality among the ex-smokers might be that many of them stopped smoking because of ill health. The mortality of persons smoking only cigarettes increased as the average amount smoked daily increased. Thus for persons smoking less than 10, 10 to 20, 21 to 39, and 40 or more cigarettes a day in 1954 the mortality ratios were 1·29, 1·67, 1·78, and 1·99 respectively. This trend was less apparent with other forms of smoking, only those persons smoking 9 or more cigars or 20 or more pipefuls of tobacco a day having a mortality materially different from that of non-smokers, the ratios being 1·44 and 1·21 respectively.

The relation between smoking and mortality from different causes was studied along similar lines, account being taken both of the underlying cause of death and contributory causes. Again the data are presented as mortality ratios, but in order to have a more stable basis of comparison the category of "occasional smokers" was combined with that of non-smokers. Among regular smokers of cigarettes only, the mortality ratio was greater than 2 for cancer of the lung (9·85), cancer of the prostate (2·17), cancer of the oesophagus and buccal cavity (2·18), bronchitis and emphysema (3·27), peptic ulcer (2·83), and cirrhosis of the liver (2·95). For cardiovascular diseases the ratios ranged from 1·33 (cerebral vascular lesions) to 1·63 (coronary heart disease). There was no material increase attributable to smoking in mortality from chronic rheumatic heart disease (0·84), chronic nephritis (1·04), or suicide and accidents (0·99). Sufficient data were not always available for the effect on mortality of the amount smoked to be determined, but for lung cancer the ratio increased from 5·50 with a consumption of less than 10 cigarettes a day to 10·00 with 10 to 20 a day and 15·80 with 21 or more a day, and a similar trend (1·00, 2·50, and 4·00 respectively) was observed for cancer of the buccal cavity and oesophagus. A lesser increase in mortality from cancer of the lung and from all forms of cancer was observed among smokers of cigars or pipes, or of both.

E. A. Cheeseman

478. **The Acute Toxic Effects of Black Smoke**

R. E. PATTLE, G. D. WEDD, and F. BURGESS. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **16**, 216–220, July, 1959. 11 refs.

At the Chemical Defence Experimental Establishment, Porton, Wiltshire, the effects of inhalation of the black smoke produced by burning tetralin in a hurricane lamp were studied in mice, rats, and guinea-pigs. Mice which died showed blackening and congestion of the lungs, and the trachea was often blocked with sooty liquid. Similar changes were seen in rats, but in the guinea-pigs there were emphysematous, haemorrhagic, and atelectatic patches in the lungs which resembled those produced by inhalation of sulphuric acid mist. Tetralin smoke

was found to be much more toxic to mice and guinea-pigs than was sulphur dioxide. Correlation of the findings with the quality of the London smog of 1952 showed that tetralin smoke in the same concentration as found in the London smog had no detectable acute effect on these animals. *John Pemberton*

479. **Blanket Laundering and Sterilization: Report of a Trial at the City General Hospital, Sheffield**
E. H. GILLESPIE and W. ROBINSON. *Journal of Clinical Pathology* [*J. clin. Path.*] **12**, 351–354, July, 1959. 8 refs.

Woollen blankets, untreated and treated to resist shrinking, cellular cotton blankets (loom state), and blankets made of Turkish towelling were laundered at the City General Hospital, Sheffield, by the techniques summarized in the table below. The reagents used for

Table of Laundering Processes

	Temperature (° C.)	Time (minutes)
Wool		
1. Wash, "syndet 54"	37·8	10
2. Rinse, water	Cold	5
3. Sterilize, "steravol"	Cold	5
4. Hydro-extraction	—	8
5. Dried on continuous belt (air temperature)	93·3–100	15
Cotton		
1. Wash, mixture:		
(a) Cotton cellular	71·1–76·6	10
(b) Turkish towelling ..	82·2–93·3	10
2. Rinse, water	Cold	6
3. Hydro-extraction	—	10
4. Dried on continuous belt (air temperature)	93·3–100	15

the woollen blankets were "syndet 54", a powdered non-ionic detergent combined with a mildly acid builder, used at the rate of 2 lb. per 70 lb. (1 kg. per 35 kg.) load, and "steravol", a quaternary ammonium compound, 2 pints per 70 lb. (1·2 l. per 35 kg.) load. For cleaning the cotton blankets a solution was made up of 800 gallons (3,636 l.) of water, 36 lb. (16·3 kg) of "escolite" (a blended product of high alkaline activity), 10½ lb. (4·76 kg.) of "comprox TL" (an anionic detergent), and 7 lb. (3·175 kg.) of pure soap.

Sweep plate cultures before laundering of all types of blankets gave counts of 300 to >500 colonies, including many pathogens. After laundering no pathogens were isolated and the average sweep plate count was no more than five colonies. Blankets laundered with "syndet 54" alone gave an average count of 16 colonies.

The authors consider that cotton cellular blankets proved the most satisfactory, being cheap, light, and warm, liked by patients and nurses, and easily sterilized by laundering at temperatures high enough to kill vegetative bacteria. It is advisable to stretch the cotton blankets during laundering, preferably while still wet. The main disadvantage of these blankets is excessive fluff, which can disseminate bacteria through a ward. Woollen blankets are satisfactory, but should be pre-shrunk. Turkish-towelling blankets are heavy and clumsy to handle and were not liked by patients or nurses. *H. Caplan*

480. **Persistence of Bacteria in the Developmental Stages of the Housefly. I. Survival of Enteric Pathogens in the Normal and Aseptically Reared Host**
B. GREENBERG. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **8**, 405–411, July, 1959. 6 figs., 11 refs.

This paper from the University of Illinois College of Pharmacy, Chicago, describes studies of the survival of human pathogenic organisms through the developmental cycle of the common housefly (*Musca domestica*). Maggots grown from untreated eggs in a normally contaminated medium were infected with test organisms, including *Shigella paradysenteriae* (*flexneri*) IIa, *Salmonella typhosa* (Vi), and *Salm. paratyphi* B. Counts of the infecting organisms were made at different stages of development. To test infectivity larvae or prepupae were picked out one day after introduction of the pathogen, disinfected in a solution of mercuric chloride, and washed in cold water and then in cold thioglycollate solution, which was incubated to demonstrate successful disinfection. The lowered temperature inhibited movement, thus reducing the possibility of recontamination of the thioglycollate from the gut. The specimens were finally ground up and incubated. Newly emerged adult flies were processed without disinfection or washing.

In 6 separate experiments *Salm. paratyphi* B was recovered from 0 to 71% of adults. In 3 of the experiments a larger proportion of larvae than of adults were infected, in 2 no organisms were recovered from either larvae or adults, and in one no organisms were recovered from larvae, although the adults were infected. In 2 out of 5 experiments with *Salm. typhosa* and in 3 out of 4 with *Shig. flexneri* organisms were recovered from a comparatively small proportion of larvae, but in none were they recovered from adults. Similar experiments using disinfected eggs and sterile media yielded different results, pathogenic organisms introduced in the early stages of development being consistently recovered from larvae and pupae of various ages, mature maggots typically harbouring about 10^7 organisms and pupae from the second day to emergence 10^3 to 10^4.

The author concludes that under normal contaminated conditions *Shig. flexneri* and *Salm. typhosa* tend to die out at some stage between the maggot and the adult. This may be due to an unfavourable environment created by the normal maggot flora, for in the absence of a competing flora the human pathogens are able not only to persist, but also to multiply. *A. E. Wright*

481. **Persistence of Bacteria in the Developmental Stages of the Housefly. II. Quantitative Study of the Host–Contaminant Relationship in Flies Breeding under Natural Conditions**
B. GREENBERG. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **8**, 412–416, July, 1959. 4 figs., 6 refs.

In further studies of the survival of bacteria in the developmental stages of the housefly [see Abstract 480] field collections of maggots, prepupae, and pupae were made during the summer from breeding grounds in horse manure, garbage, and privy contents. Daily col-

lections were made and the specimens washed, disinfected, and ground in thioglycollate solution. Bacterial counts were made from individual specimens and the organisms isolated and identified. The bacteria isolated were predominantly those of the breeding ground from which the specimen had originally been obtained, and included members of the *Proteus* and *Escherichia* groups. Mature maggots consistently yielded counts of 10^7 organisms, the count decreasing through all subsequent stages of development to between 0 and 10^6 (mostly 10^2) in newly emerged flies. The two major falls in count occurred at the prepupal stage and at the adult stage. These findings are in agreement with those of the previous experiments, in which human pathogens showed a similar pattern of survival.

The author concludes that " on the basis of the evidence presented in this and the preceding study, it is considered doubtful that the normal flora are better suited than the pathogens for survival in the gut of the developing fly ". *A. E. Wright*

482. Q Fever Studies. XXI. The Recovery of *Coxiella burnetii* from the Soil and Surface Water of Premises Harboring Infected Sheep

H. H. Welsh, E. H. Lennette, F. R. Abinanti, J. F. Winn, and W. Kaplan. *American Journal of Hygiene* [*Amer. J. Hyg.*] **70**, 14–20, July, 1959. 1 fig., 12 refs.

The investigation here reported was undertaken at the Viral and Rickettsial Disease Laboratory, Berkeley, California, in an attempt to determine whether soil and water might serve as sources of *Rickettsia burneti* in areas harbouring flocks of sheep known to be infected with Q fever. Weekly samples of soil and water were collected over a 10-month period from selected sites on 5 different ranches, and for 15 months on a sixth ranch, in Solano County. After collection, samples were stored at −20° C. until processed for inoculation into hamsters. Six weeks later the sera of inoculated animals were examined for complement-fixing antibodies with a commercial antigen prepared from the Henzerling strain of *R. burneti*.

Of 19 samples of water collected on the 6 ranches over a 6-week period during the rainy season, 6 (32%) from 3 of the ranches contained from 30 to 10,000 hamster-infective doses per ml. It appeared likely that contamination of water to this degree might easily give rise to infected aerosols under favourable circumstances. Soil samples taken from the 3 ranches where infected water was found were also positive, and on 2 of the ranches *R. burneti* was consistently recovered for periods exceeding 100 days. Contamination of the soil appeared to be greatest during the lambing season, but when the investigation was continued through the next lambing season on one ranch recoveries were more patchy. The reason for this was not apparent, but there remained a clear association between parturition and contamination of the environment.

The authors conclude that rickettsiae are able to persist for long periods, and that disturbance of dusty contaminated soil may lead to infection in man and livestock. [See also Abstract 270]. *A. E. Wright*

483. Use of Orally Administered Live Attenuated Polioviruses as a Vaccine in a Community Setting: a Controlled Study

R. N. Barr, H. Bauer, H. Kleinman, E. A. Johnson, M. M. da Silva, A. C. Kimball, and M. K. Cooney. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 893–905, June 20, 1959. 4 figs., 10 refs.

This paper reports the results of a carefully controlled study of the effects of orally administered live attenuated polioviruses which was carried out during 1958 at the University of Minnesota among married students and their families who were living in a " village " site of closely packed double prefabricated dwellings occupying 6 adjacent city blocks. A total of 551 volunteer subjects (about half the village population), consisting of 263 children of an average age of 2·4 years and 146 fathers and 142 mothers, average ages 27 and 26 respectively, participated as family units in the study. About one-fifth of the participants had previously received no Salk vaccine, these being chiefly infants under one year of age and some fathers, while just over one-half had had 3 doses. During the first 76 days of the study half the subjects selected on a random basis (Group A) were given a placebo, while the other half (Group B) received orally in gelatin capsules at 3-weekly intervals first about 100,000 T.C.D. of an attenuated MEF–1 Type-2 poliovirus, then 75,000 T.C.D. of an attenuated SM Type-1 strain, and finally 200,000 T.C.D. of the Fox Type-3 strain. During the remaining period of the 5-month study Group A received the attenuated viruses and Group B the placebo. From each subject 6 specimens of stool and 3 specimens of blood were obtained; close supervision and record-keeping both of individuals and family units were maintained throughout the study. Although numerous illnesses of various types, principally upper respiratory infections and gastro-intestinal disturbances, occurred among all the participants during the control period, there was no overwhelming preponderance of symptoms limited to either of the experimental groups and the pattern of illness was exactly the same as that occurring in the city of Minneapolis as a whole.

Many of the participants had antibodies to poliovirus in their serum at the beginning of the study, but positive responses to the vaccines occurred in almost all the children except a few of the infants under one year old. In those whose initial titres were less than 1:4 sixteenfold rises or greater were elicited in 70·3% for Type-1 virus, in 76% for Type 2, and in 70% for Type 3, while a rise in titre to all three types occurred in 85%. In the control children given the placebo who had titres of less than 1:4 a rise in titre was observed in a few instances. Virus was recovered from the stools of 4 of these children, and infection had probably occurred in 4 others as a result of interfamilial spread. Among the adults, in whom the vaccines appeared to be less effective—only 15% of those with titres of less than 1:4 showing sixteenfold increases to all three types—the differences in responses between the group given the vaccine and the placebo control group were statistically significant for all 3 types. The presence of naturally occurring anti-

bodies appeared to prevent the establishment of an intestinal infection by attenuated viruses, but the presence of serum antibodies similar to those induced by Salk vaccine did not prevent such an infection. The attenuated viruses also appeared to effect an anamnestic reaction in those who showed no evidence of having been successfully stimulated by previous use of formalinized vaccine. *A. Ackroyd*

484. **Communitywide Vaccination Program with Attenuated Poliovirus in Andes, Colombia**
H. ABAD-GÓMEZ, F. PIEDRAHITA, R. SOLÓRZANO, and M. M. DA SILVA. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 906–913, June 20, 1959. 4 figs., 20 refs.

In January, 1958, an outbreak of paralytic poliomyelitis appeared to be developing in one of the southern rural counties of the Republic of Colombia where, owing to the poor hygienic conditions generally prevailing, most children have had a poliovirus infection by the age of 2 and the paralytic form of the disease is rarely seen, the highest annual rate for poliomyelitis between 1947 and 1957 being 1·6 cases per 100,000 of the population. Because formalinized vaccine is incapable of halting the spread of poliomyelitis it was decided to vaccinate children in the more highly susceptible age groups (2 months to 6 years inclusive) with orally administered live attenuated poliovirus vaccine. As the threatened epidemic appeared to be due to virus of Type 1 $10^{4·9}$ T.C.I.D.$_{50}$ (50% tissue culture infective dose) of the attenuated SM strain of Type-1 poliovirus was given first in a hard gelatin capsule, followed at 3-weekly intervals by 2 capsules containing a total of $10^{5·3}$ T.C.I.D.$_{50}$ of attenuated MEF–1 Type-2 strain, and then a capsule of $10^{5·1}$ T.C.I.D.$_{50}$ of the Fox Type-3 strain.

In all, 94·5% of the 7,378 children under the age of 6 who received the first dose of vaccine completed the course. No undesirable reactions were observed which were associated with or attributable to the oral vaccination. In order to follow the response to vaccination samples of blood were obtained from all children between the ages of 6 months and 10 years in every 10th family among the 2,922 families participating, first before and then one month after vaccination. Initially no antibodies could be detected to any type of poliovirus in the serum of 9·7% of these 690 children, 35·5% had demonstrable antibody to one or two types, and 54·8% to all three types. Postvaccination conversion from negative to positive occurred in 91% for Type 1, in 72% for Type 2, and in 87% for Type 3, while 4-fold or greater booster responses were observed in the majority previously found to have demonstrable antibodies. Of the 58 children lacking antibodies to all three types before vaccination, all showed antibodies in the serum after vaccination. Among 18 household contacts with antibody titres of less than 1:4 conversion from negative to positive occurred in 6 out of 9 for Type 1, 2 out of 3 for Type 2, and 1 out of 6 for Type 3. Failure to respond to vaccination was most frequent for the Type-2 strain vaccine; this was probably due to interference by the Type-1 strain, which was given first, thus allowing the successful establishment of Type 2 in the intestine of those lacking antibodies to this virus. Although 4 new cases of poliomyelitis were reported in the area covered by this study after the start of the vaccination programme, none occurred in a vaccinated child or a contact of such child, and since the conclusion of the programme no further cases of the disease have been reported. *A. Ackroyd*

INDUSTRIAL MEDICINE

485. **Patterns of Sickness Absence in a Railway Population**
C. GORDON, A. R. EMERSON, and D. S. PUGH. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **16**, 230–243, July, 1959. 6 figs., 8 refs.

In this paper from the Department of Public Health and Social Medicine, University of Edinburgh, the results are reported of a study over a period of one year of the sickness absences of 14,074 Scottish railwaymen. The number of episodes of sickness per man increased only slightly with age, but the duration of each illness increased markedly with age. Episodes tended to last for a week or a completed number of weeks, and Monday was the commonest day on which the absence started. Sickness absences were of longer duration among men working where exposure to the weather was greatest than among men whose work was less exposed. It was concluded that in studying the causes of sickness absence such factors as working conditions, the man's attitude to the job, family pressure to remain at work, and loyalty to the working group must be considered. Men who eventually go off sick often work to the end of the week during which they first feel ill. *John Pemberton*

486. **Dermatitis in the South Wales Mining Industry: a Report of a Survey of Two Collieries**
B. F. MATTHEWS. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **16**, 200–207, July, 1959. 1 fig., 3 refs.

The incidence and aetiology of occupational dermatitis and other forms of skin disease in coalminers were studied in two collieries in Glamorganshire, in one of which the number of claims over an 18-month period for benefit for dermatitis under the National Insurance (Industrial Injuries) Act was high and in the other it was low. Both collieries possessed pit-head baths and medical centres. Observation of the underground environmental conditions showed no significant difference between the two. However, workmen from the "high-claim" pit lived in a moderately large mining town some distance from the place of work, whereas the men from the "low-claim" colliery lived in villages close to the pit. The number of men at each colliery was just over 1,000, and there were no great differences in the age and occupational distribution of the two groups of employees.

The cases of dermatitis found by preliminary screening were divided into three groups: (1) occupational dermatitis, which was diagnosed on the basis of a character-

istic history of a rash (often pruritic) occurring during the man's employment as a miner, evidence of improvement when not exposed to colliery conditions, and duration of the skin infection of at least 7 days; (2) non-occupational dermatitis; and (3) skin lesions of doubtful aetiology. The entire survey took place between August, 1954, and June, 1955, that at the high-claim colliery being completed in December, 1954.

Almost all the workmen at both collieries were examined. At each colliery 29 cases of occupational dermatitis were found, giving almost identical rates of 2·9% and 2·7%, and at each the condition in 27 of the 29 cases was considered to be eczema of traumatic origin. No significant difference in incidence was found between coal-face workers, other underground workers, and surface workers. The age at onset of the first attack was similar at both collieries (40 to 60 years). In coal-face workers the lesions developed most commonly on the lower limbs, while in men employed elsewhere the lesions were found usually on the hands and forearms. The average duration of exposure before initial attacks was similar at the two collieries, 27 years at the high-claim and 24 years at the low-claim colliery. The duration of attacks was also similar, the condition persisting for over 12 months in 40% of cases at each colliery. The "severity" of the dermatitis was assessed by combining the time lost during all attacks; not surprisingly, the total absence from work was greater at the high-claim colliery. The difference in the number of claims at the collieries is presumed to be a result of the difference in severity. [As this, the only difference between the two collieries, arises by selection, it implies an assumption to measure "severity" by means of absence statistics. The difference in absence rates might be related to other factors, such as home environment in town (high-claim colliery) and village environment (low-claim colliery).] *W. K. S. Moore*

487. **An Experimental Investigation of the Action of Chromite and Magnesite Dust on the Body.** (Экспериментальные исследования действия на организм пыли хромомагнезитовых и магнезитохромитовых огнеупоров)
T. A. Roščina. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] 3, 28–32, July–Aug., 1959. 2 figs., 8 refs.

Chromite and magnesite are components of new refractory materials used in metallurgy, and workers in this industry may be exposed to concentrations of several hundred mg. of dust per cubic metre having a high content of magnesium and chromium oxides and a relatively high content of aluminium oxide and silicon dioxide. Apart from reports in the literature regarding the effects of inhalation of the oxides of magnesium and chromium separately, which results in the development of "foundry fever", little work has apparently been done on the effects of the two oxides in combination. Experiments were therefore carried out on white rats, which were subjected to chronic exposure to a dust concentration of 375 to 400 mg. per c.m. for 2 hours a day for 4 months and then killed.

Post-mortem examination of the lungs of these animals showed that those exposed to magnesite developed pulmonary changes typical of the reaction to a chemically inert foreign body. Thus there was proliferation of lymphocytes and histiocytes, thickening of the interalveolar septa, very slight phagocytosis, paresis of the bronchioles, and peribronchiolar and perivascular infiltration by small round cells. In the animals exposed to chromite on the other hand there were pronounced vascular changes in the lungs, the capillaries being congested and showing hyperplasia of the endothelium, while erythrocytes and leucocytes were present in the alveoli. Fewer lymphocytes were present than in the animals exposed to magnesite and there was considerable phagocytosis of the dust. The bronchioles were in spasm. Various different mixtures of the two dusts caused combinations of proliferative and exudative changes in the lungs in proportion to the amount of each constituent present. The author therefore stresses that when the dust hazard is being assessed in connexion with the use of new refractory materials determination of the exact composition of the dust is of fundamental importance. *Basil Haigh*

488. **Fatigue Involved in Travelling between Home and Work in Workers in Paris.** (La fatigue du trajet chez les travailleurs parisiens)
V. Raymond and C. Baruch. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] 20, 349–356, July–Aug., 1959.

The contribution to fatigue made by travelling to and from work was studied in a group of 300 Paris workers, 229 men and 71 women. The subjects were mostly between the ages of 20 and 40 years and generally gave no history of previous serious disease. This notwithstanding, the examiners noted 17 cases of chronic pulmonary disease, 33 of cardiovascular disease, especially hypertension and varicose veins, and 26 of defective physique. A most striking observation was that 69 persons—66 men and 3 women—belonging mainly to the category of heavy workers, showed evidence of chronic alcoholism in the form of enlargement of the liver and muscular tremors.

Among the data recorded, and summarized in 8 tables, were the length and time of the journey before and after work, the type of transport used, the nature (light, medium, or heavy) and duration of work, and the influence of travel on eating habits. Of the 300, no fewer than 124 spent more than 1½ hours each day in getting to and from work. The amount of fatigue induced was determined less by the type of conveyance than by the amount of waiting, intermediate changing, and crowding at peak hours. Office workers and those in kindred light occupations recorded that travelling was often more exhausting than work, whereas heavy workers such as foundrymen regarded travelling as a relaxing break.

[Apart from the extent of chronic alcoholism, based on such criteria of advanced disease as enlargement of the liver and tremors, the authors' observations are common experience. The problem involves many more social and economic factors other than those embraced in this study.] *A. Meiklejohn*

Forensic Medicine and Toxicology

489. **Blood Transfusion in Carbon Monoxide Poisoning.** (О применении переливания крови при отравлении окисью углерода)
N. K. TALYZINA. *Педиатрия* [*Pediatrija*] **37**, 78–79, June, 1959. 3 refs.

Carbon monoxide poisoning is one of the deadliest menaces to life, and its effect is more rapid and more injurious in young children than in adults. Even if the patient survives, serious damage to the central nervous system may already have been caused. In this paper the author reports 6 cases of the intoxication, 2 in adults and 4 in children ranging in age from 6 months to 6 years. In addition to the usual measures all the patients were treated by venesection followed by blood transfusion with citrated blood of Group O or packed cells, to which they all responded rapidly. This procedure is recommended as being of prime importance owing to the rapid deterioration which results from the prolongation of anoxia. *L. Firman-Edwards*

490. **The Renal Response to Administration of Acetazolamide (Diamox) during Salicylate Intoxication**
R. SCHWARTZ, F. X. FELLERS, J. KNAPP, and S. YAFFE. *Pediatrics* [*Pediatrics*] **23**, 1103–1114, June, 1959. 6 figs., 15 refs.

The renal response to administration of acetazolamide in salicylate intoxication was studied in 3 patients, aged 21 months to 3½ years, admitted to the Children's Medical Center, Boston. The drug was given intravenously over a period of 1 to 2 minutes in a dosage of 3 to 6 mg. per kg. body weight. The rate of excretion of free salicylate was 35 to 300 times greater than the minimum rates during control periods, but no increase in excretion of salicylurate or other conjugates was noted. Exacerbation of the metabolic acidosis as a result of administration of acetazolamide was prevented by intravenous infusion of large quantities of sodium bicarbonate. Frequent determinations of the *p*H and the carbon dioxide content of the serum were necessary.

The authors point out that neurological complications such as papilloedema and convulsions, which occurred in 2 of the cases, may preclude the use of acetazolamide therapeutically. *Norval Taylor*

491. **Salicylate Intoxication with Special Reference to the Development of Hypokalemia**
E. D. ROBIN, R. P. DAVIS, and S. B. REES. *American Journal of Medicine* [*Amer. J. Med.*] **26**, 869–882, June, 1959. 7 figs., 37 refs.

The manifestations of salicylate intoxication are discussed with reference to the findings in 5 cases studied at the Peter Bent Brigham Hospital, Boston, and one case reported in the *British Medical Journal* (1958, **1**, 503). Initially salicylates stimulate respiration, resulting in alkalosis which causes potassium loss. This alkalosis tends to pass over into a metabolic acidosis, distinguishable from respiratory alkalosis only by the change in the *p*H of the blood, which must be determined at frequent intervals. Treatment includes intravenous administration of potassium chloride and glucose in alkalosis and of sodium bicarbonate or lactate in acidosis, with oxygen if necessary. Respiratory depressants are contraindicated. It is stated that salicylate poisoning may lead to renal failure and that it always causes a characteristic fall in uric acid content of serum and urine which can be of diagnostic value. *V. J. Woolley*

492. **Artificial Hemodialysis in Management of Glutethimide Intoxication**
B. F. CHANDLER, W. H. MERONEY, S. W. CZARNECKI, R. H. HERMAN, M. D. CHEITLIN, L. R. GOLDBAUM, and E. G. HERNDON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **170**, 914–917, June 20, 1959. 2 figs., 10 refs.

From the Walter Reed Army Hospital, Washington, D.C., the treatment of 2 cases of attempted suicide by taking glutethimide is described. The amount taken did not exceed 15 g., but both patients went gradually into deep coma. Persistence of this coma and failure of conventional treatment led to the use of a Kolff–Brigham type of haemodialysis apparatus in an effort to reduce the blood glutethimide level. In one of the cases 1,420 mg. of the drug was removed at an almost constant rate of 150 mg. per hour. Both patients recovered.
Norval Taylor

493. **The Treatment of Barbiturate Poisoning by Alkalinization of the Plasma and Urine.** (Le traitement de l'intoxication barbiturique aiguë. L'épuration par l'alcalinisation plasmatique et urinaire)
P. MOLLARET, M. RAPIN, J. J. POCIDALO, and J. F. MONSALLIER. *Presse médicale* [*Presse méd.*] **67**, 1435–1438, July 25, 1959. 5 figs., 20 refs.

The authors first point out that through the continual improvement in methods of treatment the mortality among patients with barbiturate poisoning has been progressively reduced, from 24·5% in 1945 to 20% in 1947, 14% in 1949, 4·2% in 1955, and finally to 1·4% in 1957. In their view the fundamental goal is to obtain still more rapid elimination of the poison from the body, if possible through the natural channel, namely, the kidneys. In experiments on dogs they have shown that an increase in the *p*H of the plasma hinders transfer of barbiturate from plasma to body cells and also reduces the reabsorption of barbiturate in the renal tubule.

They then describe 93 cases of barbiturate poisoning admitted to the Hôpital Claude-Bernard, Paris, of which 58 were treated by the intravenous infusion of sodium bicarbonate, 3 to 4 litres of a 1·4% solution being usually given over 24 hours; where facilities for tracheotomy or intubation are available a 3% solution may be used. In either case enough potassium chloride, 3 to 9 g. per

day, must be added to the infusion to prevent potassium depletion. It is also important to employ the usual respiratory and circulatory stimulants, but in cases treated with these alkaline infusions the addition of diuretics produces no further elimination. All the patients so treated made a good recovery. In a comparable series of 8 severely poisoned cases in which the mean dose of barbiturate ingested was known to be 6·8 g. the mean duration of coma was 7·1 days, whereas in 13 of the patients treated by alkaline infusion the mean dose was 7·7 g. and the coma lasted only a mean of 3·8 days. Thus the alkali treatment approximately halved the duration of coma as compared with treatment by the older methods. *V. J. Woolley*

494. **The Identification of Biological Stains by Immunochemical Methods.** (L'identification des taches biologiques par les méthodes immunochimiques)
M. MULLER, G. FONTAINE, and P. H. MULLER. *Annales de médecine légale et de criminologie, police scientifique et toxicologie* [*Ann. Méd. lég.*] **39**, 337–356, July–Aug. [received Oct.], 1959. 11 figs., 33 refs.

From the Institut de Médecine Légale de Lille the authors describe the use of an immunochemical method for the identification of biological stains. The two questions that arise in studying such stains concern, first, the nature of the material and, second, its origin. The first question is often simply answered by the finding of haemoglobin, sperms, epithelial cells, and so on. The method used by the authors is directed towards answering the second question, that of origin.

Methods depending on antigen–antibody reactions were introduced in 1901 and have been developed steadily since then. While such methods are theoretically unassailable, their delicacy brings practical difficulties. The risk of subjective error in interpretation is high, and cloudy media may vitiate the readings of haemolytic reactions. Moreover, without specialized techniques photographic records of the reactions may be impossible to obtain. These hazards may be avoided by mixing the immune serum with an equal amount of 4% gum acacia solution, the gel so formed being placed in a tube and the test fluid or macerated stain poured on top. The precipitate appears where the two solutions meet. The technique used by the authors is that of Ouchterlony, which is a development of this method. A thickened gel is spread on a Petri dish or photographic plate. A hole 1 cm. in diameter is cut out in the centre and filled with immune serum, and 4 peripheral holes are made 1 cm. from this reservoir to receive the test solutions. The reaction takes 2 or 3 days to complete, a positive result being shown by a line of precipitation at the point where the two liquids meet in the gel. A photographic record can be made with a camera or directly on sensitized paper. Moreover, the plate can be dried and the precipitates stained by the methods used in electrophoresis, and it is possible to store the preparation as a permanent record. The same method can be adapted for use on microscope slides with minute quantities of fluids, as described by Hartmann and Toilliez (*Rev. franç. Ét. clin. biol.*, 1957, 2, 197). The authors prefer this as a routine. In both macro- and micro-methods care is needed to exclude dust and avoid desiccation during the period of development of the reaction. The antibody used is anti-human or anti-animal serum. The authors prefer rabbit serum, though they stress the great importance of immunizing the rabbit rapidly with a minimum number of injections of antigen. The use of stock horse serum is possible, but as it is often produced after a large number of immunizations there may be troublesome cross-reactions from the multiplicity of antibodies present. A high degree of accuracy is obtained with dilutions of human blood up to 1 in 1,000, and the ability to preserve the plates is invaluable in medico-legal work. The technique can be used for human seminal stains, urine, milk, cerebrospinal fluid, and gastric contents and for identifying animal stains. By means of a similar technique electrophoresis with a weak current can be used to analyse the immunological reactions between human and animal sera in the presence of anti-human horse or rabbit serum.

[The authors describe their employment of these techniques in great detail, and workers in forensic laboratories would be well advised to read the original.]
Gavin Thurston

495. **Carbon Monoxide Determinations in Post-mortem Tissues as an Aid in Determining Physiologic Status prior to Death**
S. S. WILKS and R. T. CLARK. *Journal of Applied Physiology* [*J. appl. Physiol.*] **14**, 313–320, May, 1959. 4 figs., 11 refs.

The authors, working at the U.S.A.F. Randolph Air Force Base, Texas, have found that in an increasing number of unexplained aircraft crashes it has not been possible to decide whether the accident was due to mechanical failure of the machine or physiological failure of the crew. If the latter, one possible cause might be the accumulation of carbon monoxide (CO). Since blood is not always available after a very bad crash, or if available may have lost much of its CO content by exposure to light and air, the authors have devised a method for determining the CO content of solid tissues, the CO evolved from a sample of homogenized tissues being estimated by colour-indicator tubes, the van Slyke method, or an infra-red CO analyzer. Animal experiments and observations on patients dying in various circumstances have shown that the blood CO levels could be obtained by extrapolation from tissue CO values. It was also shown by animal experiment that burning of the tissues did not *per se* alter their CO content, and that it was unlikely that the occurrence of explosion and fire after a crash would significantly alter the CO levels in the tissues before death ensued.

Analyses of muscle tissue from 186 aircraft crash victims showed that in 32% of these subjects the tissue CO level corresponded to a blood CO level exceeding 30% saturation. In the 99 cases in which fire was known to have occurred before the crash the results differed little from those in the other 87 cases. The authors conclude that CO was present in the crew's compartment of some or all of these aircraft at some time during the flight. The possible significance of this finding is being investigated. *H. B. Stoner*

Anaesthetics

496. **Pethidine and Levallorphan: Their Combined Use for Premedication**
F. F. FOLDES, P. G. MCNALL, L. R. KOUKAL, and R. TANAKA. *Anaesthesia* [*Anaesthesia*] **14**, 255–261, July, 1959. 2 refs.

The authors report from the University of Pittsburgh School of Medicine, and Mercy Hospital, Pittsburgh, the results of an investigation designed to determine whether the routine administration of levallorphan with premedication would lessen the depressant effects of narcotics given to supplement anaesthesia. A total of 80 patients received premedication with 100 mg. of pentobarbitone and 1·5 mg. pethidine per kg. body weight, together with 0·3 to 0·4 mg. of scopolamine; 40 of the patients received, in addition, 0·02 mg. of levallorphan tartrate per kg. body weight. All the drugs were administered intramuscularly 95 to 210 minutes before the beginning of the study. After the pulse rate, blood pressure, and respiration rate had been recorded anaesthesia was induced with 5 mg. of thiopentone per kg. body weight, nitrous oxide and oxygen being administered through a face mask by a standard technique. At 4 minutes pulse rate, blood pressure, respiration rate, and minute volume were recorded. At 5 minutes 20 patients who had received levallorphan and 20 who had not were given 1 mg. of pethidine per kg. body weight by intravenous injection. The remaining 40 patients received at this time 0·4 mg. of alphaprodine per kg. body weight. Further experimental readings were taken at 8 and 12 minutes, all being recorded before the start of the operation.

It was found that thiopentone caused moderate circulatory changes which were unaffected by previous administration of levallorphan. It caused a slight increase in respiratory rate in patients who had received levallorphan and a decrease in the rate in those who had not received the antagonist. Both pethidine and alphaprodine resulted in a reduction in pulse rate, systolic pressure, respiratory rate, and minute volume. In general, the respiratory and circulatory effects were greater after alphaprodine and the protective effect of levallorphan was greater with pethidine. The antagonist provided moderate protection against the respiratory effects of the analgesics, but not against their circulatory effects. The authors consider that if an antagonist is to be used prophylactically it should be injected just before the analgesic is given. *Mark Swerdlow*

497. **High Vagal Block: Anatomy and Technic**
F. A. D. ALEXANDER. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 267–273, July–Aug., 1959. 3 figs., 10 refs.

This paper is based on the author's experience in performing, at Marcy State Hospital, New York, high vagal block on 150 occasions, this being bilateral in 100 cases and unilateral in 50. The course and anatomical relations of the vagus nerve in the jugular fossa are described in detail and well illustrated. In performing the block the patient's head is turned to the opposite side and a 50-mm. needle inserted into the crease behind the ear where the pinna joins the lateral surface of the head. On striking bone, which may be either the styloid process or the inferior portion of the vaginal plate, the needle is partially withdrawn and directed anteriorly and inferiorly until the bone is by-passed. It is then advanced 1·5 to 2 cm. until a further bony structure, the occipital condyle, is encountered; if the needle is now withdrawn a distance of 0·3 cm. its point should be in the immediate vicinity of the vagus nerve. At this point 5 ml. of 2% procaine or 3 ml. of 2% lignocaine is injected. The complications encountered in the author's series included puncture (on 21 occasions) of the internal jugular vein and in a few cases glossopharyngeal neuritis. The changes produced by vagal block and the indications for its use are described. *Mark Swerdlow*

498. **Segmental Epidural Anesthesia as the First Choice**
M. R. WESTER, L. W. KRUMPERMAN, and S. C. MESCHTER. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 178–187, May–June, 1959. 2 figs., 2 refs.

The authors have studied the value of limited segmental epidural block and now report their experience in 105 patients undergoing major surgical operations at Temple University Medical Center, Philadelphia. In this method anaesthesia is established and maintained with fractional doses of lignocaine, hexylcaine, or 2-chloroprocaine administered via an epidural catheter the tip of which is placed near the middle of the segment to be anaesthetized. The patients were mostly poor-risk cases and the operations performed included radical mastectomy, thoracic cordotomy, renal operations, Peet sympathectomy, reduction of fractured vertebrae, or operations on arteries below the level of the renal arteries. The authors discuss their results in each operation group and indicate the advantages and disadvantages of the method. The procedure failed in 6 cases and the subarachnoid space was inadvertently entered in a further 2. In the authors' hands epidural block has provided safe and effective anaesthesia in most cases, but they stress that its induction at any level above the lumbar regions demands a mastery of the technique. *Mark Swerdlow*

499. **Brachial Plexus Block for Hand Surgery**
J. W. DITZLER and R. H. CLIFFORD. *Journal of Occupational Medicine* [*J. occup. Med.*] **1**, 363–368, July, 1959. 9 refs.

The results of brachial plexus block performed in 526 cases for surgery of the hand at the Henry Ford Hospital, Detroit, are evaluated. The indications included trauma

following a recent meal, concurrent steroid therapy, diabetes mellitus, old age, and general debility. The age distribution of the patients was from 7 to 78 years, with a mean of 40 years. The supraclavicular approach was used, special care being taken to elicit paraesthesiae in the arm with the needle before injecting the anaesthetic. The preparations found most satisfactory were a solution containing 2% lidocaine (lignocaine) and 0·1% tetracaine (amethocaine) and one containing 3% 2-chloroprocaine and 0·1% tetracaine. Adrenaline was added to make a final dilution of 1 in 200,000. [The total quantities of the drugs used for the blocks are not mentioned.]

Success was obtained in 85% of cases. Pneumothorax occurred in 5 cases (less than 1%). Other complications, which occurred 17 times in all, included tenderness at the injection site, pain in the shoulder, paraesthesiae at the elbow, pain in the chest, and pain in the distribution of the ulnar and musculocutaneous nerves. The difficulties of making a useful statistical analysis of complications are outlined. The authors suggest that brachial plexus block should be reserved for patients for whom general anaesthesia is contraindicated.

J. V. I. Young

500. **The Relationship of Operative Position to the Incidence of Postspinal Headache**

G. D. Alexander, E. M. Brown, and B. J. Sivak. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 259–264, July–Aug., 1959. 29 refs.

In this study, carried out at the Sinai Hospital of Detroit, 686 patients who had undergone operation under spinal anaesthesia were questioned at intervals postoperatively and any symptoms complained of were noted. It was found that the incidence of "spinal headache" was highest (8·3%) in the small group of patients (12) operated on in the lateral position. The next highest incidence of headache (7·1%) occurred among those (341) for whom the lithotomy or jack-knife position had been employed, while headache was least frequent (1·5%) among the 333 patients operated on in the supine position. The authors discuss the probable mechanism of spinal headache and the factors influencing its occurrence, and conclude that the patient's position during operation and a reduction in the volume of the cerebrospinal fluid due to leakage are the most important.

Mark Swerdlow

501. **Hyperventilation for the Maintenance of Anaesthesia**

I. C. Geddes and T. C. Gray. *Lancet* [*Lancet*] **2**, 4–6, July 4, 1959. 3 figs., 14 refs.

Hyperventilation for the maintenance of anaesthesia is discussed in the light of the authors' experience at the Royal Liverpool United Hospitals. A very light anaesthesia is used consisting of nitrous oxide and a relaxant, thiopentone often being omitted. Pallor, sweating, and vasovagal responses after severe stimuli, which have been reported as occurring under light anaesthesia, are not observed with this technique; this is attributed to the full doses of relaxants given, complete muscle flaccidity and the effective control of respiration being achieved. It has been proved that patients with controlled respiration are almost always in a state of alkalosis. In conscious patients who are hyperventilated to the point of respiratory alkalosis, dizziness and confusion develop, often associated with characteristic waves in the electroencephalogram (EEG). These delta-type waves are also seen during anaesthesia with nitrous-oxide—relaxant and when the patient is hyperventilated. The present authors have attempted to correlate alterations in the blood *p*H with the appearance of slow-wave activity. Their anaesthetic procedure was as follows. Premedication for adult patients was with 25 mg. of promethazine and 0·65 mg. of atropine. After pre-oxygenation for 5 minutes to eliminate nitrogen a test dose of 5 mg. of tubocurarine was given and anaesthesia was induced with nitrous oxide. For maintenance the concentration of nitrous oxide was 70%—a concentration which produces narcosis but does not prevent movements in response to strong stimuli. A dose of 25 to 30 mg. of tubocurarine was given and the patient intubated, additional doses of tubocurarine being administered to allow control of respiration. This dosage was not sufficient to prevent movement, but with controlled respiration movements ceased. A two-channel portable EEG apparatus was connected to the patient before induction, and a fronto-occipital unipolar lead was used for monitoring. The *p*H of venous blood was estimated in an anaerobic three-arm assembly in a thermostatically controlled water-bath. It was found that as the *p*H rose slow-wave activity occurred, this disappearing as the *p*H fell. Slow-wave activity disappeared after carbon dioxide was introduced and returned when CO_2 was washed out. The EEG patterns of hyperventilation and of certain planes of ether and halothane anaesthesia were found to be similar.

The authors consider that in anaesthesia hyperventilation appears to be harmless and conducive to good operating conditions.

M. Woods

502. **Bemegride Termination of Out-patient Anaesthesia: the Effect upon Recovery from Thiopentone–Nitrous Oxide Anaesthesia**

J. Mackett. *Anaesthesia* [*Anaesthesia*] **14**, 248–254, July, 1959. 20 refs.

The investigation described herein was undertaken to determine whether bemegride would significantly shorten the recovery time following anaesthesia with thiopentone in a dosage of 6·2 mg. per kg. body weight. Two groups of patients were studied: the first included 100 patients undergoing manipulations for which not more than 4 minutes' anaesthesia was required and the second included a similar number undergoing manipulations for which more than 4 minutes' anaesthesia was necessary. In all cases 0·64 mg. of atropine was given by rapid intravenous injection as premedication 30 minutes before induction of anaesthesia with 6·2 mg. of thiopentone per kg. body weight, followed by nitrous oxide and oxygen (8:2). Half the patients in each group received 50 mg. of bemegride at the termination of anaesthesia.

The intervals between the end of anaesthesia and the time when the patient could (*a*) answer questions ("waking time") and (*b*) maintain a sitting posture un-

aided (" sitting time ") were estimated in all cases. In the first group there was a significant reduction in the average waking and sitting times in patients who had received bemegride. In the second group the addition of bemegride was not associated with a significant shortening of recovery time, there being a negative correlation between duration of anaesthesia and the recovery time.

The literature on the use of bemegride in anaesthesia is briefly reviewed and the variable results obtained by others are discussed in the light of the findings in the present investigation. *Mark Swerdlow*

503. **Continuous Flow Spirometry in Anaesthesia**
R. S. ATKINSON. *Anaesthesia* [*Anaesthesia*] **14**, 231–239, July, 1959. 11 figs., 5 refs.

In this paper from Chase Farm Hospital, Enfield, the author describes a spirometric technique for use in anaesthesia. A recording spirometer is inserted into the anaesthetic circuit and continuous tracings are taken of the patient's respiration. Examples of the qualitative and quantitative changes produced in the respiratory pattern under various conditions are given.

Halothane, 1%, caused a reduction of 21% in tidal volume; with this agent the response to carbon dioxide stimulation was clearly related to the depth of anaesthesia. Hydroxydione and trophenium both caused marked depression of respiration. The author noted that if time was allowed for recovery from the effects of a dose of suxamethonium subsequent injection of gallamine was not followed by an abnormal response.

Mark Swerdlow

504. **Controlled Respiration in Neurosurgical Anaesthesia**
S. GALLOON. *Anaesthesia* [*Anaesthesia*] **14**, 223–230, July, 1959. 37 refs.

Alterations in and interference with respiratory function during neurosurgical anaesthesia can have serious consequences. After listing the special requirements of anaesthesia for neurosurgery the author of this paper from the Royal Infirmary, Cardiff, describes the advantages of controlled respiration in this field. Respiratory physiology can be maintained within normal limits and coughing and straining avoided. The light level of anaesthesia reduces the amount of drugs required, minimizes the toxic effects of prolonged anaesthesia, and promotes rapid recovery of consciousness after the operation. The disadvantageous effect of controlled respiration on the circulation can be overcome by the use of a negative pressure phase during expiration. The author gives some practical details of his own technique.

Mark Swerdlow

505. **Carbon Dioxide Absorption**
G. MILES and J. ADRIANI. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 293–300, July–Aug., 1959. 1 fig., 7 refs.

The early history of carbon dioxide absorbers and the subsequent developments in their design are described. It is pointed out that the canisters in the older types of circle absorbers were theoretically too small, and the present study was therefore carried out at Louisianal State University, New Orleans, to test and re-evaluate their operating efficiency. The experiments were performed in the laboratory using a mechanical ventilator which simulates rebreathing and a Liston–Becker infrared analyser for continuous sampling of carbon dioxide. The " respiratory rate " was fixed at 20 per minute, the " tidal volume " at 525 ml., and the carbon dioxide flow rate at 200 ml. per minute. A plastic cylindrical canister of variable capacity was constructed and this was packed firmly with soda lime. The ventilator was operated so that inspiration and expiration were of equal duration, and the gases entered the canister at room temperature. When a charge of 650 g. of a 6- to 8-mesh, high-moisture type of soda lime was used absorption proceeded uniformly to reach the end-point (fixed at 0·5% CO_2 in the issuing gases) in 6 hours. Increasing the capacity of the canister lengthened the absorption time by approximately 1 hour for each additional 100 g. of soda lime. When " exhausted " lime was rested overnight and the experiment repeated the end-point was reached in 30 minutes. There was no difference between the efficiency of the canister in the horizontal position and that in the vertical position. The authors consider that with the types of soda lime now available periods of " rest " for this absorbent are unnecessary. The performance of certain individual canisters was investigated and the results are briefly described. *Mark Swerdlow*

506. **Carbon Dioxide Balance during Thoracic Surgery**
R. A. THEYE and W. S. FOWLER. *Journal of Applied Physiology* [*J. appl. Physiol.*] **14**, 552–556, July, 1959. 4 figs., 12 refs.

The authors, working at the Mayo Clinic, have investigated certain factors affecting the carbon dioxide balance during thoracic surgery, the study being carried out on 28 dogs which were anaesthetized with pentobarbitone or allobarbitone and urethane and ventilated artificially with a Starling pump. Paralysis was maintained with an infusion of suxamethonium. The following values were then determined: respiratory minute volume, oxygen uptake, CO_2 output, respiratory exchange ratio, arterial and mixed venous plasma CO_2 content, *p*H, and pCO_2, end-expiratory pCO_2, and pleural gas exchange. Observations were made first while the animals were in the supine and lateral positions with the chest closed, and then similarly with the chest open, and also following the successive ligation first of the left main bronchus and then of the left pulmonary artery.

Among the many findings, presented in a series of graphs, it was noted that the creation of an open pneumothorax was accompanied by a significant metabolic change characterized by an increase in oxygen uptake and CO_2 elimination, the cause of which was obscure. Ligation of the left main bronchus caused only a small and temporary impairment of elimination of CO_2, the pCO_2 increasing slightly in the arterial blood and decreasing slightly in the end-expiratory gas. Ligation of the pulmonary artery on the other hand resulted in

very marked changes, the arterial and mixed venous pCO_2 rising by some 10 mm. Hg, while the end-expiratory tension fell by a slightly smaller amount. Neither of the ligation procedures had any significant effect on oxygen consumption. Alterations in the respiratory exchange ratio resulted from the impairment of CO_2 elimination observed when the pulmonary artery was ligated. No exchange of gas appeared to take place through the pleura. The authors conclude that the ventilatory requirements during thoracic surgery are not significantly altered by the effects of a lateral position, open pneumothorax, or a small right-to-left shunt, but that alveolar ventilation is considerably affected by the distribution of ventilation between perfused and unperfused alveoli. *J. F. Nunn*

507. **Gaseous Exchange during Halothane Anaesthesia: the Steady Respiratory State**
J. F. NUNN and R. L. MATTHEWS. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **31**, 330–340, Aug. [received Oct.], 1959. 6 figs., 19 refs.

Using the Douglas bag technique, the oxygen uptake, carbon dioxide output and respiratory exchange ratio have been measured in 12 patients under halothane anaesthesia. The mean oxygen consumption was depressed to 83% of the basal value—a level which is comparable with other methods of anaesthesia and with natural sleep. There is thus no indication that halothane specifically causes a reduction of metabolic rate sufficient to protect the brain from interruption of its blood supply as in hypothermia. The oxygen consumption was significantly higher in the patients who were breathing spontaneously, compared with the patients who were ventilated artificially. Measurement of the carbon dioxide output and the respiratory exchange ratio showed that a period of at least 50 minutes of uniform ventilation was required to reach a steady state with regard to these parameters. In the few cases in which equilibrium was achieved, the reduction of carbon dioxide output appeared comparable with the reduction of oxygen uptake. The respiratory exchange ratios were of the order of 0·85.—[Authors' summary.]

508. **Mephentermine: Its Value as a Pressor Agent in Anaesthesia**
D. J. COLEMAN. *Anaesthesia* [*Anaesthesia*] **14**, 240–247, July, 1959. 2 figs., 25 refs.

The properties desirable in a vasopressor agent are described and the relative values of those in current use are discussed. A new agent, mephentermine, was given to 31 patients at St. George's Hospital, London, the aim being in some cases to prevent a fall in blood pressure —for example, before epidural anaesthesia—and in others to treat hypotension occurring during or after operation.

Uniformly satisfactory results were obtained with a dose of 7 to 15 mg. Marked fluctuations in blood pressure were avoided and no untoward side-effects were noted. The author considers that mephentermine is a valuable pressor agent with a wide margin of safety. *Mark Swerdlow*

509. **Venous Pressure during Anesthesia**
R. C. MCPHERSON, E. OGDEN, and J. J. JACOBY. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 306–312, July–Aug., 1959. 28 refs.

Venous pressure was measured in 27 patients [at Ohio State University Hospital] immediately before induction of anesthesia, after induction of anesthesia, and at the end of the surgical procedures while the patients were still fully anesthetized. The drugs used included thiopental, curare, cyclopropane, nitrous oxide, and ether. In 19 patients, changes in cardiac output were determined by ballistocardiography. In 6 patients, oscillometric studies also were done.

Venous pressure was rather consistently elevated during induction and during the course of anesthesia. The increase in venous pressure was not associated with any constant change in cardiac output as indicated by the ballistocardiogram, arterial blood pressure, or oscillometric amplitude. The increase in peripheral venous pressure was regularly associated with engorgement of superficial veins in anesthetized patients. The increase in venous pressure and the engorgement of superficial veins probably were due to the negatively inotropic effect of the anesthetic agents and to a redistribution of blood flow and blood volume in the extremities.—[Authors' summary.]

510. **Cardiac Conduction Disturbances during Anesthesia in the Uremic Patient**
C. I. COMPAMANES, C. P. BOYAN, W. S. HOWLAND, and J. W. BELLVILLE. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 283–288, July–Aug., 1959. 20 refs.

At the Memorial Center for Cancer and Allied Diseases, New York, the authors have studied the disturbances in cardiac function arising during anaesthesia in 108 patients undergoing nephrostomy, of whom 88 had a raised blood urea level preoperatively, while the remaining 20 with a normal blood urea level served as controls. Estimation of the serum potassium level in 64 of the former patients showed that this was raised in 43, whereas in all the control patients the serum potassium level was normal. Tachycardia developed in 13 of the 88 patients, 7 of these having a raised serum potassium level. Bradycardia was noted in 3 patients and cardiac arrest occurred in 3, all 6 of whom had a raised serum potassium level. Arrhythmia arose in 5 patients, in 3 of whom the potassium level was increased. Disturbances in cardiac conduction were commonest when cyclopropane was the agent employed. None of the control cases exhibited impaired cardiac conduction. The mechanisms of these cardiac irregularities and the influence thereon of various anaesthetic agents and adrenaline are discussed at length. *Mark Swerdlow*

511. **A Physiological Approach to the Problem of General Anaesthesia and of Loss of Consciousness**
W. FELDBERG. *British Medical Journal* [*Brit. med. J.*] **2**, 771–782, Oct. 24, 1959. 18 figs., bibliography.

Radiology

512. **X-ray Treatment of Sequelae of Penetrating Cranial Injuries with Foreign Bodies Embedded in the Brain.** (Применение рентгенотерапии при последствиях проникающих ранений черепа (при наличии инородных тел в веществе головного мозга))
E. I. ROZENBLIT and M. E. MANIKOV. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] **34**, 49–53, July–Aug., 1959. 7 refs.

It has been the authors' experience that radiotherapy for the relief of post-traumatic symptoms of penetrating cranial injuries is not contraindicated, even in the presence of embedded foreign bodies. In such cases, however, the single doses of x rays must not exceed 25 to 50 r., these being given every 4 to 7 days to a total dose amounting to between 300 and 600 r. In several of the authors' patients relief of symptoms, such as headaches and epileptic fits, was observed immediately, and persisted for several years. They found, however, that in cases in which foreign bodies were present in the sensorimotor zone of the cortex x-ray therapy was of little avail. *A. Orley*

RADIODIAGNOSIS

513. **Dynamic Encephalography**
E. C. PALMA. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 992–1000, June, 1959. 10 figs., 29 refs.

Encephalography is usually avoided in patients with raised intracranial pressure, it being considered that ventriculography is safer in these circumstances. However, in this paper from Montevideo, Uruguay, a method is described which it is claimed is effective and safe in such cases. It is as follows. A high cisternal puncture is made with the needle directed obliquely upwards to enter the cisterna magna at the upper margin of the foramen magnum between the cerebellar tonsils. Since the lower ends of the tonsils are below the point of the needle, the column of cerebrospinal fluid (C.S.F.) filling the spinal canal thus remains intact at all times, supporting the tonsils. Between 8 and 20 ml. of oxygen is rapidly injected and radiographs taken precisely at the moment of completion. The syringe is immediately removed to allow the escape of oxygen or C.S.F., thus relieving the very temporary increase of pressure caused by the injection. The process is repeated as necessary. Filling of the third and fourth ventricles and the aqueduct occurs if no obstruction exists, while at the same time the basal and posterior-fossa cisterns are delineated. If obstruction does exist its site is demonstrated, together with any displacement or deformity.

This technique has been carried out on a total of 170 patients with only one fatal accident. On the whole it has been well tolerated, but not unexpectedly headache, nausea, and vomiting are encountered in some cases. The method is said to cause fewer complications than lumbar encephalography, and it is claimed that the danger of cerebellar herniation into the foramen magnum is minimized. In cases in which there is very high intracranial pressure, and so in which the danger of tentorial cerebral hernia exists, a previous decompression is performed by inserting a cannula into one of the lateral ventricles. *Arnold Appleby*

514. **Cisternal Pneumoencephalography**
S. MULLAN and A. PINEDA. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 984–991, June, 1959. 5 figs., 12 refs.

From the University of Chicago Clinics comes this communication describing the authors' experience and technique of introducing air into the ventricles by cisternal puncture. The results are compared briefly with those of pneumoencephalography performed via the lumbar route. For cisternal pneumoencephalography the patient sits in a special chair, leaning backwards in a semi-reclining position but with the neck moderately flexed so that Reid's base line is horizontal. The puncture is made in the usual way, except that the needle is pointed slightly upwards. Air is slowly introduced over 3 to 5 minutes until some headache is complained of. In the average case 20 to 25 ml. gives an adequate result. If headache is encountered during the injection of the first 10 ml. this probably means that the air is not entering the ventricles; in such a case radiographs are taken to ascertain the true state of affairs and the head is repositioned or the examination abandoned. No fluid is withdrawn as a rule until the introduction of air has been completed. The patient is then laid prone and the usual views taken.

A total of 72 patients have been examined in this way, of whom 11 had intracranial tumour, only 2 of these having papilloedema. The impression gained was that the side-effects of the investigation were relatively mild; headache rarely persisted to the next day and in no case did the patient's condition deteriorate following the examination. In general, lumbar encephalography necessitated the use of greater volumes of air and produced more disturbance in the 46 cases in which it was employed. The failure rate was less than 10% by either method, good ventricular filling being obtained in the remainder. It is pointed out that because of the proximity of the medulla oblongata this procedure is not one for the inexpert, nor is its use advocated in every case. The lumbar route is preferable in cases of cerebral atrophy, suprasellar and parasellar tumours, and those of the cerebello-pontine angle. The authors consider, however, that cisternal encephalography is the method of

choice for the location of cerebral tumours when intracranial pressure is not raised. They suggest that it may even be preferable to ventriculography in cases of tumour with raised intracranial pressure, and quote figures reported from England and Germany indicating that it is safer than ventriculography in such cases. If tonsillar herniation is already present no fluid will of course be obtained and the method is then impossible of performance. *Arnold Appleby*

515. **Positive Contrast Ventriculography**
M. C. WILSON and S. R. SNODGRASS. *Radiology* [*Radiology*] 72, 810–815, June, 1959. 4 figs., 10 refs.

In the course of neuroradiological investigation it is sometimes necessary to obtain unequivocal visualization of the third ventricle, the aqueduct of Sylvius, and the fourth ventricle. This can usually be achieved by means of pneumoencephalography or by tomography, but there will remain a small number of cases in which even these methods fail. In this event it is possible to fill the small midline ventricular cavities with a contrast material of high density such as " pantopaque " so that the ventricular outlines stand out clearly. Although the technique, termed positive contrast ventriculography, has been known for 30 years, it has not been widely used in the U.S.A., and the authors now report from the University of Texas Medical Branch, Galveston, their experience of the method.

Except in infants it is necessary to introduce the contrast medium through burr holes in the skull. By this route 1 to 2 ml. of pantopaque is injected—the amount depending on the estimated size of the third ventricle as assessed in previous air studies—and the medium manipulated into the desired positions under fluoroscopic control. The method has been found of great value in infants with non-communicating hydrocephalus, since the limited amount of gas or air which can be introduced into the greatly dilated ventricular system of such patients without seriously affecting their general condition often fails to demonstrate the third ventricle, aqueduct, and fourth ventricle. In 11 of the authors' cases, of which 4 are described in detail, stenosis of the aqueduct was revealed with a frequency and certainty not possible by other methods. *J. MacD. Holmes*

516. **Pantopaque Ventriculography in the Localization of Surgical Lesions of the Posterior Fossa**
B. L. RALSTON, S. W. GROSS, and C. W. NEWMAN. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 972–983, June, 1959. 5 figs., 16 refs.

Ventriculography with " pantopaque " (" myodil ", ethyl iodophenylundecanoate) as contrast medium has been fairly widely used for some time, but this communication from the Mount Sinai Hospital, New York, describes a technique for this investigation which obviates the necessity for screening. In this, 3 ml. of myodil is injected into a lateral ventricle through a burr hole (preferably frontal) so that it forms a pool in the frontal horn. The patient is laid prone on a tilting table with the neck in the neutral position and his head is then gradually extended until the orbito-meatal line is horizontal. This allows the myodil to flow backwards along the floor of the lateral ventricle and drop through the foramen of Monro into the third ventricle. Over-extension of the head is to be avoided, since this will cause loss of the medium through the aqueduct and fourth ventricle into the subarachnoid space. The patient is then turned into the supine position by assistants while the operator holds the head so that neither too much extension nor too much flexion occurs, as over-extension now results in myodil flowing back into the lateral ventricles, while over-flexion causes loss of medium into the subarachnoid space. The head is then gently flexed allowing the medium to fill the aqueduct and fourth ventricle. At this point antero-posterior and lateral films are exposed. Air is introduced at the same time as the myodil and this outlines the lateral ventricles and the anterior end of the third ventricle, while the posterior end of the third ventricle, the aqueduct, and the fourth ventricle are outlined by the myodil.

The authors report that this technique gave successful delineation of the aqueduct and fourth ventricle in over 30 cases with surgical lesions of the posterior fossa, permitting precise location of the lesion. They point out however that accurate location of posterior-fossa tumours is sometimes possible by fractional air encephalography and that in the absence of such a lesion satisfactory visualization of the third and fourth ventricles and aqueduct is often obtained. Pantopaque ventriculography therefore is not recommended as an initial measure, but should be resorted to only after air encephalography has failed to give a satisfactory demonstration, thus sparing many patients the necessity of having burr holes made. A few cases are quoted to illustrate the accuracy of the method. Only transient reactions to the opaque medium were noted, in spite of the use of rather larger amounts than usual.

[While the correct manipulation of the head probably requires practice, the method described in this paper appears to offer an attractive alternative to fluoroscopy in the upright position, often in drowsy, uncooperative patients.] *Arnold Appleby*

517. **Pantopaque Myeloencephalography**
R. MONES and R. WERMAN. *Radiology* [*Radiology*] 72, 803–809, June, 1959. 6 figs., 7 refs.

From the Mount Sinai Hospital, New York, the authors describe a new neuroradiological procedure for the demonstration of abnormalities of the posterior fossa and upper cervical region. By this technique, which they term myeloencephalography, the third and fourth ventricles, the cisterna magna, and the posterior rim of the foramen magnum can be visualized by the injection of 9 to 12 ml. of " pantopaque " into the lumbar subarachnoid space, as in the routine performance of myelography. The spinal needle being removed, the patient in the supine position is then tilted head-down under fluoroscopic control to an angle of 45 to 55 degrees. The fourth ventricle, cisterna magna, and posterior aspect of the third ventricle can be recognized quickly since

they usually fill within a few minutes. Antero-posterior and lateral films are then taken and the patient returned to the horizontal position, where another series of antero-posterior and lateral films are exposed. The procedure is said to be simple and to entail much less manœuvring than routine cervical myelography.

Of 40 cases so examined, the posterior rim of the foramen magnum was visualized in all. In 2 cases in which the cisterna magna did not fill it was later shown that abnormalities of the posterior fossa were present in both—platybasia in one case and a cerebellar medulloblastoma in the other. In 31 cases the cerebellar tonsils were identified. Of 5 of these cases in which the tonsil border was well below the foramen magnum, a cerebellar tumour was present in 4.

Ventricular filling corresponds generally to the success or failure of pneumoencephalography. In this series the fourth ventricle was filled in 23 cases; among the 17 cases in which there was no ventricular filling, 11 showed a mass in the posterior fossa, and 10 of these had shown no filling on pneumoencephalography. Information which was given by myeloencephalography but not by pneumoencephalography in this series was as follows: displacement of the 4th ventricle (3 cases); normal 4th ventricle (1); obstruction of the aqueduct (1); herniated cerebellar tonsils (5); and absence of filling of the cisterna magna (2 cases). The procedure was found to produce less discomfort for the patient, and an undesired reaction characterized by fever, pleocytosis, and meningeal signs which lasted less than a week occurred in only one of the 40 patients. *J. MacD. Holmes*

518. **Cine-angiocardiography**

R. Astley, C. G. Parsons, and A. L. d'Abreu. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **52**, 457–459, June, 1959. 8 figs., 3 refs.

Between August, 1954, and November, 1958, the authors recorded a total of 254 cine-angiocardiograms and 37 cine-aortograms; in this paper they analyse their findings in 109 cine-angiocardiograms taken during the last 14 months of this period. They state that patent ductus arteriosus is quickly and accurately diagnosed by this method, and as the development of symptoms often means a poor prognosis they suggest that in every infant with symptoms of a left-to-right shunt cine-angiocardiography should be carried out to exclude this easily curable condition. In the series of 109 cine-angiocardiograms there were 14 instances of a patent ductus. A diastolic dilution defect in the enlarged pulmonary artery is the most typical and constant sign. Septal defects in infancy are easily differentiated from a patent ductus by venous injection in the left oblique position. When the right heart fills a dilution defect is seen in the right atrium or ventricle and when the left heart fills there is refilling of the right heart. To demonstrate septal defects after infancy cine-angiocardiography is best employed in conjunction with selective injection during cardiac catheterization. Pulmonary stenoses—valvular, infundibular, or combined—are best demonstrated in the right oblique position by a venous or selective injection. The timing of events seen on the cine-angiocardiogram may be accomplished by taking it simultaneously with an electrocardiogram or pressure tracing on which the time of exposure of each cine frame is recorded.

In general the authors prefer the cine technique to large-film angiocardiography, but consider that the latter is indicated when a larger field area is required—for example, to show multiple collateral vessels—or when small detail has to be demonstrated.

Michael C. Winter

519. **Cine-aortography for the Visualization of the Aortic Valve and Coronary Arteries**

G. Sloman. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **52**, 460–461, June, 1959. 2 figs., 6 refs.

With the increasing use of a direct-vision approach in the surgical treatment of diseased aortic valves an accurate preoperative assessment of the anatomy and function of the valves has become important. The author, writing from St. George's Hospital, London, describes a method of cine-aortography which was tried on 25 dogs and subsequently applied clinically in 8 patients. In the clinical trial a No. 8 NIH catheter was inserted through the right brachial artery into the ascending aorta until its tip was about 2 cm. above the aortic valve. The contrast medium was injected and films taken in the left anterior oblique position at 32 frames per second.

The author suggests that cine-aortography with a standard 5-inch (12·7-cm.) image intensifier is indicated as follows: (1) in aortic stenosis and regurgitation to study the movement of the aortic valve leaflets and to assess approximately any aortic regurgitation; (2) in mitral valve disease when an early diastolic murmur is heard at the base of the heart cine-aortography will exclude aortic regurgitation; (3) to define the anatomy of aneurysms of the ascending aorta or of the sinuses of Valsalva; and (4) to visualize the level of various forms of aortic fistulae. When the field size can be increased, so that a complete coronary angiogram can be obtained, cine-aortography may help in the diagnosis of chest pain when the electrocardiogram is normal, in established coronary arterial disease to assist in prognosis and to evaluate treatment, and in objective assessment in patients selected for myocardial revascularization.

Michael C. Winter

520. **Body Section Roentgenography in the Evaluation and Differentiation of Chronic Hypertrophic Emphysema and Asthma**

R. G. Fraser and D. V. Bates. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **82**, 39–62, July, 1959. 23 figs., 42 refs.

Simple methods of radiography have not been found of great value in differentiating the hypertranslucent lung which is due to chronic emphysema from that which is due to bronchospasm or spasmodic asthma. Since the alveoli of the lung in the former condition have undergone irreversible destructive changes in contrast to the relatively benign nature of bronchospasm, the authors considered that a radiological technique

which would distinguish these conditions would be of value.

Basing their work on the reported finding that in true emphysema there is a progressive narrowing of the calibre of the pulmonary arteries, they examined 43 patients by means of body-section radiography of the chest. Two or three cuts in the coronal plane at or near the hila generally sufficed to show the character of the vascular tree. Various pulmonary function tests were also carried out, the results being correlated with the radiological findings. One of the authors assessed both the plain radiographs and the sectional views without knowledge of the patients or the results of the clinical and pulmonary function tests, 3 separate assessments being made.

Of 26 patients with clinical evidence of chronic pulmonary emphysema, 21 showed a significant tapering-off of the pulmonary vessels, indicating emphysema. In a further 2 cases emphysema was assessed on 2 out of the 3 occasions. In contrast the presence of emphysema was diagnosed from the plain chest radiographs in only 8 of the 24 cases for which these radiographs were available.

Of 11 cases with clinical evidence of spasmodic asthma the assessment of the tomograms was normal in 10 and doubtful in one. A further group of 6 cases in which the clinical picture was not clear-cut and there were certain conflicting findings were also examined. Emphysema was diagnosed on the sectional radiographs in 2 out of the 6 cases.

The authors conclude that body-section radiography is a comparatively simple and helpful method of differentiating hypertrophic emphysema from asthma.

A. M. Rackow

521. **The Pathological Basis of the Radiological Changes in Ulcerative Colitis: a Study of Cases Treated by Colectomy**

A. P. Dick, F. R. Berridge, and M. J. Grayson. *British Journal of Radiology* [*Brit. J. Radiol.*] **32**, 432–449, July, 1959. 9 figs., 12 refs.

The authors, working at Addenbrooke's Hospital, Cambridge, have studied 10 cases of ulcerative colitis which were all severe enough to require colectomy and had all been treated with steroids. Radiological studies were made a few days before excision and again afterwards, and also of the colon filled with a barium enema, after its evacuation, and again after insufflation of air. Sections of the excised colon, after fixing in the distended position, were also examined.

Narrowing of the calibre of the colon, particularly in the post-evacuation films, was found to be due to fibrosis of a fairly severe nature in the submucosa with, in some cases, an extension into the muscular coat. It did not appear to be related to the duration of the disease, being seen in some cases of only 3½ to 6 months' duration. Fibrosis, however, was not always associated with narrowing. Contractility was reduced in those cases showing narrowing and fibrosis, but sometimes was still present in those with severe narrowing. Mucosal haustra are not often seen in the normal colon when distended, but nevertheless absence of haustra in the present cases correlated well with severe submucosal damage and with submucosal fibrosis, though the authors suggest that this may not be always so. The absence of mucosal haustra was not related to the presence of mucosal or submucosal inflammation. Muscular haustration was poorly seen in 2 cases only, and even these showed some narrowing, submucosal inflammation, and fibrosis. A smooth mucosal contour gave no indication of the underlying pathological abnormality, the same appearances being seen with a normal mucosa as with a completely denuded one. It is important to compare this change with changes seen in the radiographs taken after evaluation in which the important signs are the absence of mucosal haustra and an abnormal calibre. In 2 cases a few small indentations were found to be due to the presence of debris. When indentations are larger and more numerous they indicate the presence of islands of inflamed or regenerating mucosa between areas of denudation and ulceration. Areas of translucency seen in combination with a honeycomb appearance on the post-evacuation films always indicate the presence of pseudo-polyps which, however, may be present without being detected radiologically. There was no correlation between the degree of reduction of contractility and the acuteness of the inflammation. Double contours were seen in only one case and indicated the presence of active acute inflammatory ulcers, the barium tracking under their edges.

Examination after air insufflation was carried out in 9 of the cases, but in only one segment did it reveal a lesion not seen in the other films. However, double contours and mucosal haustra were shown better on such films, but the pseudo-polyps and islands were less well visualized. It was noted that the radiological changes in the irrigated excised sections of colon were more marked than the preoperative changes *in situ*, showing that the changes revealed by a barium enema appear to be less severe than they actually are, this being due to the difficulty in achieving adequate preparation of the colon in this disease.

[This is an important paper which should be read by all interested in ulcerative colitis.] *A. Gordon Beckett*

522. **Hydronephrosis following Retrograde Pyelography**

J. W. Hope and A. J. Michie. *Radiology* [*Radiology*] **72**, 844–849, June, 1959. 3 figs., 2 refs.

Intravenous pyelography was carried out on 14 patients suffering from a urinary tract infection or haematuria at the Children's Hospital of Philadelphia; this was followed by retrograde pyelography and finally by repeat intravenous pyelography within 16 hours. In 9 of the children the second intravenous pyelogram showed some hydronephrosis, which was severe in one, moderate in 4, and slight in 4. The authors attribute the renal impairment to ureteric trauma, which is more likely to occur when there is difficulty in inserting the catheter and in children. They state that they now rarely advise a retrograde pyelogram.

[These examinations were carried out in 1953, before the present emphasis on reducing the dosage of x rays.]

D. E. Fletcher